

METHODS AND COMPOSITIONS FOR INCREASING

ANTIBODY PRODUCTION

Reilly et al. Attorney Docket P1957R1

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1 GAATCAACT TCTCCATCT TTGGTAAAG AAATACAGAC ATGAAAATC TCATTGCTGA GTTGTTATTT AAGCTTGCC AAAAAGAAGA AGAGTGAAT
CTTAAGTTGA AGAGGTATGA AACCTATTCC TTATGTCG TACTTTTAG AGTAAGGACT CAACATATA TTGGAACGGG TTTTCTTCT TCTCAGCTTA

101 GAAGTGTG CGCAGGTAGA AGCTTTGGAG ATTATCGTCA CTGCATGCT TCGCATATG GCGAATAATG ACCAACAGG GTTGATTGAT CAGGTAGAGG
CTTGACAC GGTCCATCT TCGAAACCTC TAATAGCAGT GAGTTACGA AGCGTTATAC CGGTTTAC TGGTTGTGC CAACTAAC TAACATCTCC

201 GGGCGCTGA CGAGGTAAAG CCCGATGCCA GCATTCTGA CGACGATAG GAGCTGTGC GCGATTACGT AAGAAGTTA TTGAAGCATC CTCGTGAGTA
CCCGGACAT GCTCCATTTC GGGTACGCT GGTAGGACT GTGCTATGC CTCGACGAG CGCTAATGCA TTCTTCAAT AACTTCGTAG GAGCAGTCAT

301 AAAAGTTAAT CTTTCAACA GCTGTATTA AGTTGCACG GCGGAGACT ATAGTCGCT TGTGTTTAT TTTTAATGA TTTGTAAC TAACGCAAGT
TTTTCAATTA GAAAGTTGT CGACAGTATT TCAACAGTGC CGGCTGGA TATCAGCGAA ACAAATATA AAATATGAT CATGCGTTCA

401 TCACGTAAA AGGTATCTA GAATTATGA GAAGATATC GCATTCTTC TTGCTATCTAT GTTCGTTTT TCTATTGCTA CAAACGGTA CCGTATATC
AGTGCATTT TCCCATAGAT CTTAATCTT CTTCTTATAG CGTAAGAAG AACGTAGATA CAAGCAAAA AGATAACGAT GTTTGCGCAT GCGACTATAG

1 M K K N I A F L L A S M F V F S I A T N A Y A D I
~STII Signal Sequence TIR-1 Anti-Tissue Factor Light Chain~

501 CAGATGACC AGTCCCGAG CTCCTGTGTC GCGTGTGG GCGATAGGT CACCATCAC TCGCAGCCA TCGCGACAT CAAGACTAT CTGAACGTGT
GTCTACTGG TCAGGGGCTC GAGGACAGG CGGACACAC CCGTATCCA GTGGTAGTG AGCTCTCGT CAGCGCTGA GTTCTCGATA GACTTGACCA

26 Q M T Q S R S S L S A S V G D R V T I T C R A S R D I K S Y L N W Y

601 ATCAACAGAA ACCAGGAAA GCTCCGAAAG TACTGATTTA CTATGCTACT AGTCTGCTG TCGAGTCCC TTCTCGCTTC TCTGGATCCG GTTCTGGAC
TAGTTGCTT TGGTCTTTT CGAGGCTTTC ATGACTAAT GATAGATGA TCAGACGAC TTCTCAGG AAGACGAA AGACCTAGGC CAAGACCTG

60 Q Q K P G K A P K V L I Y A T S L A E G V P S R F S G S G S G T

701 GGATTACACT CTGACCATCA GCAGTCTGCA GCGAAGAG TCCGCACTT ATTACTGTCT TCAGCAGCA GAGTCTCCAT GGACATTTGG ACAGGGTACC
CCTAATGTGA GACTGGTAGT CGTCAGACGT CGGTCTTCTG AAGCTTGA AAGCTTGA TAATGACAGA AGTCTGCTCT CTAGAGGTA CCTGTAACC TGTCCCATGG

93 D Y T L T I S S L Q P E D F A T Y Y C L Q H G E S P W T F G Q G T

801 AAGGTGGGA TCAACGAAAC TGTGGCTGCA CCATCTGTCT TCATCTTCCC GCGATCTGAT GAGCAGTTGA AATCTGGAAC TCGTCTGTT GTGTGCTGC
TTCCACCTCT AGTTGCTTG ACACCGACGT GGTAGACAGA AGTAGAGGG CGGTAGACTA CTGCTCACT TTAGACCTTG ACGAAGACAA CACACGACG

126 K V E I K R T V A A P S V F I F P P S D E Q L K S G T A S V V C L L

901 TGAATPACTT CTATCCAGA GAGGCCAAG TACAGTGGAA GGTGATPAC GCGCTCAAT CCGTAACTC CCAGGAGAGT GTCACAGAGC AGGACAGCA
ACTTATTGAA GATAGGTCT CTCCGTTTC ATGTCACCTT CCACCTATTG CCGGAGTTA GCGGAGTTA GGTCTCTCA CAGTCTCTCG TCCTGTGTT

160 N N F Y P R E A K V Q W K V D N A L Q S G N S Q E S V T E Q D S K

1101 GGACGACCC TACAGCCTCA GAGCACCCT GACGCTGAGC AAGCAGACT ACGAAGAA CAAGTCTAC GCGTGGAA TCACCCATCA GCGCTGAGC
CCTGTGCTGG ATGTGGAGT CGTCGTGGGA CTGCGACTCG TTTGCTGTA TGTCTTTGT GTTTCAGAT CGGACGCTTC AGTGGGTAGT CCGGACTCG

193 D S T Y S L S S T L T L S K A D Y E K H K V Y A C E V T H Q G L S

1101 TCGCCGCTCA CAAAGAGCTT CAAAGGGGA GAGTGTAAAT TAAATCCTCT ACGCCGAGC CATGCTGGC AGCTCGGTAC CCGGGGATCT AGGCTAAGC
AGCGGGCAGT GTTCTCGAA GTTGCTCCCT CTCACAA TAATTAGAGA TCGGCGCTGC GTAGACCGC TCGAGCCATG GCGCCCTAGA TCGGATTC

226 S P V T K S F N R G E C O

FIG. 1A

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1201 CTCGGTTGCC GCGGGGCGTT TTTTATTGTT GCCAGCGCG ATCTCGAATG AACTGTGTGC GCAGGTAGAA GCTTTGGAGA TTATCGTCAC TGAATGCTTT
GAGCCAACGG CCGCCCGCAA AAAATAACHA CCGGTGCGCG TAGAGCTTAC TTGACACAGC CGTCCATCTT CGAAACCTCT AATAGCACTG ACGTTACGAA

1301 CGCAATATGG CGCAAAATGA CCAACAGCGG TTGATTGATC AGGTAGAGG GCGGTGTATC GAGTAAAGC CCGATGCCAG CATTCTCTAC GAGATACGG
CGGTATATACC CGGTTTTACT GGTGTGCGC AACTAAGTAG TCCATCTCCC CCGGACATG CTCGATTTGC GGTACGGTC GTAGGACTG CTGCTATGCC

1401 AGCTGCTGG CGATTACGTA AAGAAGTTAT TGAAGCATCC TCGTCAGTAA AAGTTAATC TTTTCAACAG CTGTCTATAA GTTGTCAAG CCGAGACTTA
TCGACGACGC GCTAATGCAT TTCTTCAATA ACTTCGTAGG AGCAGTCAIT TTTCATTTAG AAAAGTTGTC GACAGTATTT CAACAGTGCC GGCTCTGAAT

1501 TAGTGCCTTT GTTTTATTTT TTTAATGTAT TTGTAACATG TAGCGAAGTT CAGCTAATAA GGTATCTAG AATTATGAAG AAGAATATCG CATTCTTCT
ATCAGCGAAA CAATAATATAA AAATTACATA AACATTGATC ATCGGTTCAA GTGCATTTTT CCCATAGATC TTAATACTTC TTCTTATAGC GTAAAGAAGA
M K K N I A F L L
*STII Signal Sequence TIR-1

1601 TGCATCTATG TTGTTTTTTT CTAATGCTAC AAACCGTAC GCTGAGTTTC AGCTGGTGA GTCTGGGGT GGCTGGTGC ACCAGGGGG CTCACTCGT
ACGTAGATAC AAGCAAAAAA GATAACGATG TTGCGCATG CGACTCCAAG TCGACCACT CAGACCGCCA CCGACACAGC TCGGTCCCCC GAGTGAGCA
10 A S M F V F S I A T N A Y A E V Q L V E S G G L V Q P G G S L R
*Anti-Tissue Factor Heavy Chain

1701 TTGTCCTGTG CAGCTTCTGG CTTCAATATT AAGAGTACT ACATGCACTG GTTCGCTCAG GCCCGGGTA AGGCCCTGA ATGGTTTGA TTGATTGATC
AACAGACAC GTCAAGACCC GAAGTTATAA TTCTCTATGA TGTACGTGAC CAGGCGATC CGGGCCCAT TCCCGACCT TACCAACCT AACTAAGTAG
43 L S C A A S G F N I K E Y Y M H W V R Q A P G K G L E W V G L I D P

1801 CAGAGCAAG CAACACGATC TATGACCGA AGTTCACGA CCGTGCCACT ATAAGCGTG ACAATTCCAA AAACACAGCA TACTTCGACA TGAACAGCCT
GTCTGCTTCC GTTGTGCTAG ATACTGGCT TCAAGTCTCT GGACGCTGA TATTCGCGAC TGTTAAGTT TTTGTGCTGT ATGGAGTCT ACTTGTGGA
77 E Q G N T I Y D P K F Q D R A T I S A D N S K N T A Y L O M N S L

1901 GCGTGTGAG GACACTGCG TCTATTATTG TGCTCGAGAC ACGCCGCTT ACTTCGACTA CTGGGGTCAA GGAACCTGG TCACCGTCTC CTCGCCCTCC
CGCAGACTC CTGTGACGC AGATAATAC ACGAGTCTG TGCCGCGCAA TGAAGCTGAT GACCCGAGT CTTTGGACC AGTGGCAGAG GAGCCGGAGG
110 R A E D T A V Y Y C A R D T A A Y F D Y W G Q G T L V T V S S A S

2001 ACCAAGGCC CATCGTCTT CCGCTTGGA CCGTCTCCA AGACACTC TGCGGCGACA GCGGCCCTGG GCTGCTGGT CAAGGACTAC TTCCCGGAAC
TGTTTCCCG GTAGCCAGAA GGGGACCGT GGGAGGAGT TCTGTGAG ACCCCGCTGT CCGCGGACC CGACGGACCA GTTCTGTATG AAGGGCTTG
143 T K G P S V F P L A P S S K S T S G G T A A L G C L V K D Y F P E P

2101 CGGTGACGT GTCGTGAAAC TCAGGCGCC TGACAGCGG CCGTCAACAC CCGTCAACAC CCGGCGCTGG GCTGCTGGT CAAGGACTAC TTCCCGGAAC
GCCACTGCA CAGCACCTG AGTCCGCGG ACTGTCGCC CACGTGTGG AAGGGCGAC AGGATGTGAG GAGTCTGAG ATGAGGAGT COTCGACCA
177 V T V S W N S G A L T S G V H T F P A V L Q S S G L Y S L S S V V

2201 GACTGTGCC TCTACAGCT TGGGACCCA GACCTACATC TCCAACGTGA ATCACAAGCC CAGCAACACC AAGGTGGACA AGAAGTTGA GCCCAATCT
CTGACACGG AGATCGTGA ACCGTGGT CTGATGTAG ACGTTGCACT TAGTGTTCGG GTCTGTGG GTCCACCTGT TCTTCAACT CGGTTTAGA
210 T V P S S S L G T Q T Y I C N V N H K P S N T K V D K K V E P K S

2301 TGTGACAAA CTCACATG CCCACCTGC CCAGCACCTG AACTCTGGG GGGACCGTCA GTCTTCTCT TCCCGCCAAA ACCCAAGGAC ACCCTCATGA
ACACTGTTT GAGTGTATC GGTGGCAG GGTCTGGAC GTCTGGAC CCCTGGAGT CAGAGGAGA AGGGGGTTT TGGGTTCTG TGGGAGTACT
243 C D K T H T C P P C P A P E L L G G P S V F L F P P K P K D T L M I

2401 TCTCCCGGAC CCTGAGTGC ACATGCGTGG TGGTGGACGT GAGGCACGAA GACCTGAGG TCAAGTTCAA CTGTACGTG GAGGGCGTG AGGTGCATAA
AGAGGGCTG GGGACTCCAG TGTAGGACC ACCACCTGA CTCGGTGTCT TGGGACTCC AGTTCAAGT GACCATGCAC CTGCGGACC CTCACGTATT
277 S R T P E V T C V V D V S H E D P E V K F N W Y V D G V E V H N

FIG. 1B

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2501 TCCCAAGACA AAGCGCGGG AGGAGCAGTA CAACAGCAGC TACCGTGTGG TCACGCTCCT CACCGTCTTG CACGAGGACT GGCTGAATGG CAAGAGTAC
ACGGTTCTGT TTGCGCGGCC TCCTCGTCAT GTTGTGTC ATGCACACC AGTCGAGGA GTGGCAGGAC GTGGTCTCTGA CCGACTTACC GTTCTCTATG
310 A K T K P R E E Q Y N S T Y R V V S V L T V L H Q D W L N G K E Y
2601 AAGTCAAGG TCTCAACAA AGCCTCCCA GCGCCCATCG AGAAACCAT CTCCAAGCC AAAGGCGAGC CCCGAGAACC ACAGGTGTAC ACCCTGCCCC
TTCAGTTCC AGAGTTGTT TCGGAGGGT CCGGGGTAGC TCTTTGGTA GAGTTTCGG TTTCGCTGG GGGCTCTTGG TGTCACATG TGGGACGGGG
343 K C K V S N K A L P A P I E K T I S K A K G Q P R E P Q V Y T L P P
2701 CATCCCGGA AGAGATGACC AAGAACCAGG TCAGCTGAC CTGCTGTGTC AAAGGTTCT ATCCAGCGA CATGCCGCTG GAGTGGGAGA GCAATGGGCA
GTAGGCCCT TCTCTACTGG TTCTTGCTCC AGTCGACTG GACGACCAG TTTCGGAAGA TAGGTCGCT GTAGCGGAC CTCACCTCTC GTTACCCGT
377 S R E E M T K N Q V S L T C L V K G F Y P S D I A V E W E S N G Q
2801 GCGGAGAAC AACTACAAGA CCAGCCTCC CGTGTGGAC TCCGACGGCT CTTTCTTCT CTACAGCAAG CTCACCGTGG ACAAGAGCAG GTGGCAGCAG
CGCCTCTTG TTGATGTTCT GTTGGGAGG GCACGACCTG AGGCTGCCGA GGAAGAAGGA GATGCTGTC GAGTGGCACC TGTCTCTGTC CACCTCTGTC
410 P E N N Y K T T P P V L D S D G S F F L Y S K L T V D K S R W Q Q
2901 GGGACGCTCT TCTCATGCTC CGTGATGCAT GAGGCTCTGC ACAACCACTA CAGCAGAAG AGCCTCTCCC TGTCTCCGGG TAAATAAGCA TCCGACGGCC
CGCTTGCGA AGAGTACGAG GCACTACGTA CTCCGAGAGG TGTTGTGAT GTGGCTCTC TCGGAGAGG ACAGAGGCC ATTTATTCGT ACGCTGCCGG
443 G N V F S C S V M H E A L H N H Y T Q K S L S L S P G K O
3001 CTAGAGTCCC TAACGCTCGG TTGCGCGCGG GGGTTTTTA TTGTTAACTC ATGTTTGACA GCTTATCATC GATAAGCTTT AATGCGGTAG TTTATCACAG
GATCTCAGG ATTGGAGCC AACGCGGCC CGCAAAAAT AACRAATTGAG TACAAACTGT CGAATAGTAG CTATTGNA TTAGGCCATC AATATAGTGC
3101 TTAATTTGCT AACGCAGTCA GGCACCGGT ATGAAATCTA ACAATGCGCT CATGTCATC CTCGCGCCG TCACCTGGA TGCTGTAGGC ATAGCTTGG
AATTTAACGA TTGCTCAGT CCGTGGCACA TACTTTAGAT TGTTACGCGA GTAGCACTAG GAGCGGTGGC AGTGGGACCT ACGACATCCG TATCCGAACC
^Start Tet Resistance Coding Sequence
3201 TTATGCCGT ACTGCCGGC CTCTTGGGG ATATCGTCCA TTCCGACAGC ATGCCAGTC ACTATGGCT GCTGTAGCG CTATATGCGT TGATGCAAT
AATACGCCA TGACGCCCG GAGAACGCC TATAGCAGT AAGGCTGTG TAGCGTCTAG TGATACCGCA CGACATCGC GATATACGCA ACTACGTTAA

3301

FIG. 1C

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1 GAATTCACACT TCTCCATACT TTGGATAAGG AAATACAGAC ATGAAAATC TCATTGCTGA GTTGTATTTT AAGCTTGCCC AAAAAGAAGA AGAGTCGAAT
CTTAAGTTGA AGAGGTATGA AACCTATTCC TTTATGCTCG TACTTTTAG AGTAACGACT CAACAATAA TTGGAACGGG TTTTCTTCTT TCTCAGCTTA

101 GAACTGTGTG CGCAGGTAGA AGCTTTGGAG ATTATCGTCA CTGCAATGCT TCGCAATATG GCGCAAAATG ACCAACACAGC GTTGATTGAT CAGGTAGAGG
CTTGACACAC GCGTCCATCT TCGAAACCTC TAATAGCAGT GACGTTACGA AGCGTTATAC CGCGTTTTAC TGCTGTGCG CAACTAACTA GTCCATCTCC

201 GGGCGCTGTA CGAGGTAAG CCCGATGCCA GCATTCCTGA CGACGATACG GAGCTGCTGC GCGATTACGT AAAGAAGTTA TTGAAGCATC CTGTCAGTA
CCCGCGACAT GCTCCATTTC GGGCTACGGT CGTAAGGACT GCTGCTATGC CTCGACGACG CGCTAATGCA TTTCTTCAAT AACTTCGTAG GAGCAGTCAT

301 AAAAGTTAAT CTTTTCACAA GCTGTCATAA AGTTGTACG GCCGAGACTT ATAGTCGCTT TGTTTTATTT TTTTAATGTA TTTGTAACATA GTAGCGCAAT
TTTTCAATTA GAAAAGTTGT CGACGATATT TCAACAGTGC CGGCTCTGAA TATCAGCGAA ACAAATAA AAAATTACAT AAACATTGAT CATCGGTTCA

401 TCACGTAAAA AGGTATCTA GAATTATGAA GAAAAACATC GCTTTTCTTC TTGCATCTAT GTTCGTTTTT TCTATTGCTA CAAACGCGTA CGCTGATATC
AGTGCAATTT TCCCATAGAT CTTAATACTT CTTTGTGAG CGAAAAGAG AAGCTAGATA CAAGCAAAA AGATAACGAT GTTTGCGCAT GCGACTATAG

1 M K N I A F L L A S M F V F S I A T N A Y A D I
^start STII signal TIR-2 start light chain^

501 CAGATGACCC AGTCCCGCAG CTCCTCTGTC GCCTCTGTTG CGATAGGTT CACCATCACC TGCAGAGCCA GTGCGGACAT CAAGAGCTAT CTGAACCTGGT
GTCTACTGGG TCAGGGGCTC GAGGGACAGG CGGAGACACC CGCTATCCCA GTGGTAGTGG ACGTCTCGT CAGCGTGTA GTTCTCGATA GACTTGACCA

26 Q M T Q S P S S L S A S V G D R V T I T C R A S R D I K S Y L N W Y

601 ATCAACAGAA ACCAGGAAAA GCTCCGAAAG TACTGATTTA CTATGCTACT AGTCTCGCTG AAGAGTCCC TTCTCGCTTC TCTGGATCGG GTTCTGGGAC
TAGTTGTCTT TGGTCTTTT CGAGCTTTC ATGACTAAAT GATACGATGA TCAGAGCGAC TTCCTCAGG AAGAGCGAAG AGACCTAGSC CAAGACCCTG

60 Q Q K P G K A P K V L I Y A T S L A E G V P S R F S G S G S G T

701 GGATTACACT CTGACCATCA GCAGTCTGCA GCCAGAAGAC TTCGCAACTT ATTACTGTCT TCAGCACGGA GAGTCTCCAT GGACATTTGG ACAGGGTACC
CCTAATGTA GACTGGTAGT CGTCAGACGT CGGTCTTCTG AAGCGTTGAA TAATGACAGA AGTCTGCTCT CTCAGAGGTA CCTGTAAACC TGTCCTCATGG

93 D Y T L T I S S L Q P E D F A T Y Y C L Q H G E S P W T F G Q G T

801 AAGTGGAGA TCAACGAAC TGTGCTGCA CCATCTGTCT TCATCTTCCC GCATCTGAT GAGCAGTTGA AATCTGGAAC TGCTTCTGTT GTGTGCTGC
TTCCACCTCT AGTTTGCTTG ACACCGACGT GGTAGACAGA AGTAGAAGGG CGGTAGACTA CTGCTCAACT TTAGACCTTG ACGAAGACAA CACACGGACG

126 K V E I K R T V A A P S V F I F P P S D E Q L K S G T A S V V C L L

901 TGAATAACTT CTATCCAGA GAGGCCAAG TACAGTGGAA GGTGATTAAC GCCCTCAAT CGGTAACTC CCAGGAGAGT GTCACAGAGC AGGACAGCAA
ACTTATTGAA GATAGGTCT CTCCGGTTTC ATGTCACCTT CCACCTATTG CGGAGGTTA GCCCATTGAG GGTCTCTCTCA CAGTGTCTCG TCCTGTCTGT

160 N N F Y P R E A K V Q W K V D N A L Q S G N S Q E S V T E Q D S K

1001 GGACAGCACC TACAGCCTCA GCAGCACCTT GACGTGAGC AAGCAGACT ACGAACAACA CAAAGTCTAC GCCTGGGAAG TCACCCATCA GGGCCTGAGC
CCTGTGCTGG ATGTGCGAGT CGTGTGGGA CTGCGACTCG TTTGCTCTGA TGCTCTTGT GTTTCAGATG CGGACGCTTC AGTGGGTAGT CCCGACTCG

193 D S T Y S L S S T L T L S K A D Y E K H K V Y A C E V T H Q G L S

FIG. 2A

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1001 GGACAGCACC TACAGCCTCA GCAGCACCTT GAGCGTGAGC AAGCAGACT ACAGAGAAACA CAAAGTCTAC GCGTGGGAG TCACCCATCA GGGCGTGAGC
CCTGTGCTGG ATGTCGAGT CGTCGTGGGA CTGCGACTCG TTCTGTCTGA TCTCTTTGT GTTTCAGATG CGGACGCTTC AGTGGGTAGT CCCGGACTCG
193 D S T Y S L S S T L T L S K A D Y E K H K V Y A C E V T H Q G L S

1101 TCGCCCGTCA CAAAGAGCTT CAACAGGGGA GAGTGTAAAT TAAATCCTT AGCCCGGACG CATCGTGCG AGCTCGGTAC CCGGGGATCT AGGCCTAAACG
AGCGGGCAGT GTTCTCGAA GTTGTCCCTT CTCACAAATTA ATTAGGAGA TCGGGGCTGC GTAGCACCGC TCGAGCCATG GGGCCCTAGA TCCGGATTGC
226 S P V T K S F N R G E C O

1201 CTCGGTTGCC GCGGGGCGTT TTTTATTGTT GCGGACGCGC ATCTCGAATG AACTGTGTGC GCAGGTAGAA GCTTTGGAGA TTATCGTCAC TGCAATGCTT
GAGCCACGCG CGGCCCGCAA AAAATAACAA CGGCTGCGG TAGAGCTTAC TTGACACACG CGTCCATCTT CGAAACCTCT AATAGCAGTG ACGTTACGAA

1301 CGCAATATGG CGCAAAATGA CCAACAGCGG TTGATTGATC AGGTAGAGGG GCGGTGTATC GAGGTAAGC CGATGCGCAG CATTCCTGAC GACGATACGG
GCGTTATACC GGGTTTACT GGTGTGCGC AACTAATAG TCCATCTCCC CGCGACATG CTCCATTTGCG GGCTACGGTC GTAGGACTG CTGCTATGCC

1401 AGTGTGCTGG CGATTAGGTA AGAAGTTAT TGAAGCATCC TCGTCAGTAA AAGTTAATC TTTTCAACAG CTGTCAATAA GTTGTACAG CCGAGACTTA
TCGACGACGC GCTAATGCAT TTCTCAATA ACTTCGTAGG AGCAGTCATT TTCAATTAG AAAAGTTGTC GACAGTATTT CAACAGTGCC GGCTCTGAAT

1501 TAGTCGCTTT GTTTTATTT TTTAATGTAT TTGTAAGTAG TACGCAAGTT CACGTAAAAA GGGPATCTAG AATTATGAG AAAAACATCG CTTTCTTCT
ATCAGCGAAA CAAAATAAAA AAATTACATA AACATTGATC ATGCGTTCAA GTGCATTTT CCATAGATC TTAATACTTC TTTTGTAGC GAAAAGAAGA
1 M K K N I A F L L
^start Still signal TIR-2

1601 TGCATCTATG TTCGTTTTTT CTATTGCTAC AAACGGGTAC GCTGAGGTTT AGCTGGTGA GTCTGGCGGT GGCCTGGTGC AGCCAGGGGG CTCACTCCGT
ACGTAGATAC AAGCAAAAAA GATAACGATG TTTCGCGATG CGACTCCAAG TCGACCACTT CAGACCGGCA CCGGACCAAC TCGGTCCGCC GAGTGAGGCA
10 A S M F V F S I A T N A Y A E V Q L V E S G G L V Q P G S L R
^start heavy chain

1701 TTGTCCTGTG CAGTTCTGTG CTTCAATATT AAGGATACT ACATGCACTG GGTCCGTGAG GCGCCGGGTA AGGGCTTGA ATGGTTTGA TTGATTGATC
AACAGGACAC GTCGAAGACC GAAGTTATAA TTCTCTATGA TGTACGTGAC CCAGGACATC CGGGGGCCCAT TCCCGGACCT TACCCAACTT AACTAACTAG
43 L S C A A S G F N I K E Y Y M H W V R Q A P G K G L E W V G L I D P

1801 CAGAGCAAGG CAACACGATC TATGACCGGA AGTTCAGGA CCGTGCCACT ATAAGCGCTG ACATTTCCAA AAACACAGCA TACCTGCAGA TGAACAGCCT
GTCTCGTTCC GTTGTGCTAG ATACTGGCT TCAAGTCTT GGCACGTTGA TATTGCGTAC TGTAAAGTT TTTGTGTCTG ATGACGCTCT ACTTGTGGA
77 E Q G N T I Y D P K F Q D R A T I S A D N S K N T A Y L Q M N S L

1901 GCGTGTGAG GACACTGCCG TCTATTATTG TGCTCGAGAC ACGSCCGCTT ACTTGACTA CTGGGTCAA GGAACCTTG TCACCGTCTC CTCGGCCTCC
CGCACGACTC CTGTGACGGC AGATAATAAC ACGAGTCTG TGCCGGCGAA TGAAGTGAT GACCCCAAGT CCGTGGGACC AGTGGCAGAG GAGCCGAGG
110 R A E D T A V Y Y C A R D T A A Y F D Y W G Q G T L V T V S S A S

2001 ACCAAGGCC CATCGGTCTT CCCCTGGCA CCTCTCTCA AGACACCTC TGGGGCACA GCGGCCCTGG GCTGCTGTGT CAAGGACTAC TTCGCCGAAC
TGGTTCCGGG GTAGCCAGAA GGGGACCGT GGGAGGAGT TCTGTGAG ACCCCGCTGT CCGCCGGACC CGACGGACCA GTTCTGATG AAGGGCTTG
143 T K G P S V F P L A P S S K S T S G G T A A L G C L V K D Y F P E P

2101 CGGTGACGGT GTCGTGGAAC TCAGGCGGCC TGACCAAGCG CGTGACACAC TTCCCGGCTG TCCTACAGTC CTCAGGACTC TACTCCCTCA GCAGGTGGT
GCCACTGCCA CAGCACTTG AGTCCCGGG ACTGTGCGC GCAGTGTGG AAGGCCGAC AGGATGTGAG GAGTCTGAG ATGAGGAGT CGTGCACCA
177 V T V S W N S G A L T S G V H T F P A V L Q S S G L Y S L S S V V

FIG. 2B

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2101 CGGTGACGGT GTCTGGAAC TCAGGCGCCC TGACGACCG CGTGACACCC TTCCGGCTG TCCTACAGTC CTCAGSACTC TACTCCCTCA GCACGCTGGT
GCCACTGCCA CAGCACTTGG AGTCCGCGGG ACTGTCGCC GCACGTGTGG AAGGCCGAC AGGATGTCAG GAGTCTCTAG ATGAGGGAGT CGTCGCACCA
177 V T V S W N S G A L T S G V H T F P A V L Q S S G L Y S L S S V V
2201 GACTGTGCC TCTAGCAGT TGGGCACCCA GACCTACATC TGCAACGTGA ATCAACGCC CAGCAACACC AAGTGGACA AGAAAGTTGA GCCCAAATCT
CTGACACGGG AGATCGTCA ACCCGTGGT CTGGATGTAG AGTTGCACT TAGTGTGG GTCTGTGG TTCCACCTGT TCTTCAACT CGGTTTTAGA
210 T V P S S S L G T Q T Y I C N V N H K P S N T K V D K K V E P K S
2201 TGTGACAAA CTCACACATG CCCACCGTGC CCAGCACCTG AACTCTGG GGGACCGTCA GTCTCTCT TCCCCCAA ACCCAAGGAC ACCCTCATGA
ACACTGTTT GAGTGTGTAC GGGTGGCAGG GTCTGTGGAC TTGAGGACCC CCTGGGAGT CAGAAAGAGA AGGGGGTIT TGGGTCTCTG TGGGAGTACT
243 C D K T H T C P P C P A P E L L G G P S V F L F P P K P K D T L M I
2401 TCTCCGGAC CCCTGAGTGC ACATGCTGG TGTGGACCT GAGCCAGAA GACCTGAGG TCAAGTTCAA CTGTACCTG GACGGCTGG AGTGCATPAA
AGAGGCGCTG GGGACTCCAG TGTACGCACC ACCACTGCA CTCGGTCTT CTGGACTCC AGTTCAAGTT GACCATGCAC CTGCCGACCC TCCACGTATT
277 S R T P E V T C V V D V S H E D P E V K F N W Y V D G V E V H N
2501 TGCCAAAGACA AAGCGCGGG AGGAGCASTA CAACAGCAG TACCGTGTGG TCAGGTCTT CACCGTCTG CACCAAGACT GGCTGAATGG CAAGGAGTAC
ACGGTCTGT TTGCGCGCCC TCCTCGTCA GTTGTGTGC ATGGCACACC AGTGCACAGA GTGGCAGGAC GTGTCTCTGA CCGACTTACC GTTCTCTCATG
310 A K T K P R E E Q Y N S T Y R V V S V L T V L H Q D W L N G K E Y
2601 AAGTGAAGG TCTCAACAA AGCCCTCCA GCGCCATCG AGAAACCAT CTCAAAGCC AAAGGCGAG CCGAGAGACC ACAGGTGTAC ACCCTGCCCC
TTACGTTCC AGAGTTGTT TCGGGAGGT CGGGGAGTAC TCTTTTGGTA GAGTTTCGG TTTCCTGTCG GGGTCTTGG TGTCACATG TGGGACGGGG
343 K C K V S N K A L P A P I E K T I S K A K G Q P R E P Q V Y T L P P
2701 CATCCCGGA AGAGTACC AAGAACCGG TCAGCTGAC CTGCTGTGC AAAGCTTCT ATCCAGCGA CATCGCCCTG GAGTGGAGA GCAATGGGA
GAGGGCCCT TCTCTACTG TTCTTGTCC AGTCGACTG GAGGAGCAG TTTCGAGA TAGGTGCT GTAGCGGAC CTCACCTCT CGTTACCCGT
377 S R E E M T K N Q V S L T C L V K G F Y P S D I A V E W E S N G Q
2801 GCGGAGAAC AACTACAAGA CCACGCTCC CGTGTGGAC TCGACGGCT CTTCTTCT CTACAGCAAG CTCACCGTGG ACAAGAGCAG GTGGCAGCAG
CGGCTCTTG TTGATGTTT GTGCGGAGG GCACGACCTG AGGCTGCCGA GGAAGAAGA GATGCTTC GAGTGGCACC TGTTCTCGTC CACGTCGTC
410 P E N N Y K T T P P V L D S D G S F F L Y S K L T V D K S R W Q Q
2901 GGGAACTCT TCTATGCTC CGTATGCTC GAGCTCTGC ACAACACTA CACGACAGG AGCTCTCC TGTCTCCGG TAAATAAGCA TGGACGGCC
CCCTTGACA AGAGTACGAG GCACTACGTA CTCGAGAGTA GTTGTGTAT GTGCTCTTC TCGGAGAGG ACAGAGGCC ATTTATCGT ACGTGGCCG
443 G N V F S C S V M H E A L H N H Y T Q K S L S L S P G K O
3001 CTAGAGTCC TAACGCTCG TTGCGCGCG GCGTTTTTA TTGTTAACTC ATGTTGACA GCTTATCATC GATTAAGCTTT AATGCGGTAG TTTATCACAG
GATCTCAGG ATTGCGAGC AACGGCGGCC CGCAAAAT AACAACTG TACAATGAG TCAAACTGT CGAATAGTAG CTATTCGAAA TTACGCCATC AATAGTGTG
3101 TTAATTTGCT AACGAGTCA GGCACCTGT ATGAATCTA ACAATGCT CATGCTATC CTCGGCACCG TCACCTGGA TGCTGTAGG ATAGGCTTGG
AATTTAAGA TTGCTCAGT CCGTGGCACA TACTTAGAT TGTACCGA GTAGCAGTAG GAGCCGTGGC AGTGGAGCT ACGACATCCG TATCCGAAAC
3201 TTATGCGGT ACTGCGGGC CTCTGCGGG ATATGTTCA TT
AATACGGCCA TGACGGCCG GAGAACGCC TATACAGGT AA

FIG. 2C

METHODS AND COMPOSITIONS FOR INCREASING
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1 GAATTCAACT TCTCCATACT TTGGATAAGG AAATACAGAC ATGAAAAATC TCATTGCTGA GTTGTATT TTAGCTTGCC AAAAAGAAGA AGAGTCGAAT
CTTAAGTTGA AGAGGTATGA AACCTATTCC TTATGCTG TACTTTTAG AGTAACGACT CAACAATAA TTGGAACGGG TTTTCTTCT TCTCAGCTTA

101 GAACTGTGTG CGCAGGTAGA AGCTTTGGAG ATTATCCTCA CTGCAATGCT TCGCAATATG GCGCAAAATG ACCAACAGCG GTTGATTGAT CAGGTAGAGG
CTTGACACAC GGTCCATCT TCGAAACCTC TAATAGCAGT GAGCTTACGA AGCGTTATAC CGCGTTTAC TGGTTGTGCG CAACTAATA GTCCATCTCC

201 GGGCGCTGTA CGAGGTAAAG CCCGATGCCA GCATTCTCTGA CGACGATACG GAGCTGCTGC GCGATTACGT AAAGAAGTTA TTGAAGCATC CTCGTGAGTA
CCCGGACAT GCTCCATTTT GGGCTACGGT CGTAAGGACT GCTGCTATGC CTCGACGACG CGCTAATGCA TTCTTCAAT AACTTCGTAG GAGCAGTCAT

301 AAAAGTTAAT CTTTTCACCA GCTGTCAATA AGTTGTACAG GCGGAGACTT ATAGTCGCTT TGTTTTATT TTTTAAATGA TTTGTAATA GTACGCAAGT
TTTTCAATTA GAAAGTTGCT CGACAGTATT TCACAGTGC CGGCTCTGAA TATCAGCGAA ACAAATAA AAAATTACAT AAACATTGAT CATGCGTTCA

401 TCACGTAAA AGGGTATCTA GAATTATGAA GAAGATATC GCATTCTTC TTGCATCTAT GTTCGTTTT TCTATTGCTA CAAACGCGTA CCGTGATATC
AGTGCATTTT TCCCATAGAT CTTAATACTT CTTCCTATAG CGTAAGAAG AACGTAGATA CAAGCAAAA AGATAACGAT GTTTGGCAT GCGACTATAG

1 M K K N I A F L L A S M F V F S I A T N A Y A D I
*STII Signal TIR -1 Anti-VEGF Light chain^

501 CAGTTGACCC AGTCCCGAG CTCCTGTGTC GCGTAGGGT CACCATCACC TCGACGGCAA GTCAGGATAT TAGCAACTAT TTAACACTGGT
GTCAACTGGG TCAGGGGCTC GAGGGACAGG CGGAGACACC CGCTATCCCA GTGCTAGTGG AGCTGCGTT CAGTCTTATA ATCGTTGATA AATTGACCA

26 Q L T Q S P S S L S A S V G D R V T I T C S A S Q D I S N Y L N W Y

601 ATCAACAGAA ACCAGGAAA GCTCGAAAG TACTGATTTA CTTCACCTCC TCTCTCACT CTGAGTACC TTCTGCTTC TCTGATCCG GTTCTGGAC
TAGTTGCTT TGGTCCITTT CGAGGCTTTC ATGACTAAAT GAAGTGGAG AGAGAGTGA GACCTCAGG AAGAGCGAAG AGACCTAGCG CAAGACCTTG

60 Q Q K P G K A P K V L I Y F T S S L H S G V P S R F S G S G S G T

701 GGATTTCACT CTGACCATCA GCAGTCTGCA GCGAAGAG TTCGCAACTT ATTACTGTCA ACAGTATAGC ACCGTGCGGT GGACGTTTGG ACAGGTATCC
CCTAAAGTGA GACTGGTAGT CGTCAGACGT CGGTCTCTCG AAGCGTTGAA TAATGACAGT TGTCTATATCG TGGCACGGCA CTGCAAAACC TGTCCCATGG

93 D F T L T I S S L Q P E D F A T Y Y C Q Q Y S T V P W T F G Q G T

801 AAGGTGGAGA TCAACGAAAC TGTGGGTGCA CCATCTGTCT TCATCTTCCC GCACTCTGAT GAGCAGTTGA AATCTGGAAC TGTCTCTGTT GTGTGCCCTGC
TTCCACCTCT AGTTTGCTTG ACACCGACGT GGTACACAGA AGTAGAAGG CGGTAGACTA CTCGTCACT TTAGACCTTG ACGAAGACAA CACACGACG

126 K V E I K R T V A A P S V F I F P P S D E Q L K S G T A S V V C L L

901 TGAATACTT CTATCCAGA GAGGCCAAAG TACAGTGAA GGTGGATAAC GGCCTCCAAT CGGTAACTC CCAGGAGAGT GTCACAGAGC AGGACAGCAA
ACTTATTGAA GATAGGTCT CTCCGGTTTC ATGTCACCTT CCACCTATTG CGGGAGGTTA GCCATTGAG GGTCTCTCTA CAGTGTCTCG TCCTGTCTGT

160 N N F Y P R E A K V Q W K V D N A L Q S G N S Q E S V T E Q D S K

1001 GGACAGCAC TACAGCCTCA GCAGCACCTT GACGTGAGC AAAGCAGACT ACGAAGAA CAAGTCTAC GCGTGGAA TCACCCATCA GGGCTGAGC
CCTGTCTGG ATGTCGAGT CGTCGTGGA CTGCACTCG TTTGCTGTA TGTCTTTGT GTTTCAGATG CGGACGCTTC AGTGGGTAGT CCGGACTCG

193 D S T Y S L S S T L T L S K A D Y E K H K V Y A C E V T H Q G L S

1101 TCGCCCGTCA CAAAGAGCTT CAACAGGGA GAGTGTAAAT TAAATCTCT AGCCGAGC CATCGTGGC AGTCTGGTAC CCGGGATCT AGGCTTAACG
AGCGGAGT GTTCTCGAA GTTGCCCTCT CTCACATTA ATTTAGAGA TCGCGCTGCG GTAGACCCG TCGAGCCATG GCGCCCTAGA TCCGATTGC

226 S P V T K S F N R G E C O

FIG. 3A

METHODS AND COMPOSITIONS FOR INCREASING
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1201 CTGGTTGCC GCGGGCGTT TTTTATTGTT GCGGAGCGC ATCTCGAATG AACTGTGTGC GCAGGTAGAA GCTTTGGAGA TTATCGTCAC TGCAATGCTT
GAGCCAACGG CGGCCGCAAA AAAATAACAA CGGCTCGCG TAGAGCTTAC TTGACACAG CGTCCACTCT CGAAACCTCT AATAGCAGTG ACGTTACGAA

1301 CGCAATATGG CGCAAAATGA CCAACAGCGG TTGATTGATC AGGTAGAGGG GGGCTGTATC GAGGTAAAGC CCGATGCCAG CATTCCTGAC GACGATACGG
GGTTATACC GGGTTTACT GGTGTGCGC AACTAATAG TCCATCTCCC CCGGACATG CTCCATTTCG GGCTACGGTC GTAGGAGCTG CTGCTATGCC

1401 AGCTGCTGG CGATTACGTA AGAAGTTAT TGAAGCATCC TCGTCAGTAA AAGTTAATC TTTTCAACAG CTGTCTATAA GTTGTACAGG CCGAGACTTA
TGACGACGC GCTAATGCAT TTCTTCAATA ACTTCGTAGG AGCAGTCATT TTTCAATTAG AAAAGTTGTC GACAGTATTT CAACAGTGCC GGCTCTGAAT

1501 TAGTGCCTTT GTTTTATT TTAAATGAT TTGTAAGTAG TACGCAAGTT CAGTAAATA GGTATCTAG AATTATGAG AAGAATATCG CATTTCTTCT
ATCAGCGAAA CAAAATAAAA AAATTACATA AACATTGATC ATGCGTTCAA GTGCATTTT CCATAGATC TTAATACTTC TTCTTATAGC GTAAAGAAGA
M K K N I A F L L
*STII signal TIR-1

1601 TGCATCTATG TTGTTTTTTT CTATTGCTAC AAACGGTAC GCTGAGTTC AGTGTGGA GTTGGCGGT GGCTGGTGC AGCCAGGGG CTCACTCGT
ACGTAGATAC AAGCAAAA GATAAGATG TTGCGCATG CGACTCCAAG TCGACCCT CAGACCGCA CCGGACCAAG TCGGTCCCC GAGTGAGCA

10 A S M F V F S I A T N A Y A E V Q L V E S G G L V Q P G G S L R
*Anti-VBGF Heavy Chain

1701 TTGTCTCTG CAGCTTCGG CTAGACTTC AGCACTAG GTATGAAGT GGTCTGTAG GTCCTGGTGA GTTGGCGGT GGCTGGTGC AGCCAGGGG CTCACTCGT
AACAGACAC GTCAAGACC GATGCTGAAG TCGGTGATGC CATACTGAC CCAGGAGTC GGGGCCCT TCCGGACCT TACCAACCT ACCTAATGT

43 L S C A A S G Y D F T H Y G M N W V R Q A P G K G L E W V G W I N T

1801 CCTATACCG TGAACCGACC TATGCTCGG ATTTCAAAG TCGTTTCACT TTTTCTTTAG ACACCTCAA AAGCACAGA TACCTGCAGA TGAACAGCT
GGATATGCC ACTTGGCTGG ATAGAGGCC TAAAGTTGC AGCAAGTGA AAAAGAAATC TGTGAGGTT TTGTTGCTGT ATGGAGTCT ACTTCTCGGA

77 Y T G E P T Y A A D F K R R F T F S L D T S K S T A Y L Q M N S L

1901 GCGCGTGA GACACTGCG TCTATTACT TGCAAAGTAC CCGTACTATT ACGGACGAG CCACTGGTAT TTGACGCTCT GGGGTCAAG AACCTGCTC
CGCGGACTC CTGTAGCGC AGATAATGAC ACGTTTATG GGAATATAA TGCGTGCTC GGTGACATA AAGCTGCAGA CCCCAGTTCC TTGGGACGAG

110 R A E D T A V Y Y C A K Y P Y Y Y G T S H W Y F D V W G Q G T L V

2001 ACCGTCTCT CCGCTCCAC CAAGGGCCCA TCGGTCTTC CCCTGGCAC CTTCTCAAAG AGCACTCTG GGGGCACAGC GGCTCTGGC TGCTGTGTA
TGGCAGAGA GCGGAGGTG GTTCCCGGT ACCAGAGG GGAACCTGG GAGGAGTTC TCGTGAGAC CCGGTGTG CCGGACCGG ACGGACCACT

143 T V S S A S T K G P S V F P L A P S S K S T S G G T A A L G C L V K

2101 AGGACTACT CCGGAACCG GTGACGGTGT CGTGAACTC AGGCGCCTG ACCAGCGGG TGCACACCTT CCGGCTGTC CTACAGTCT CAGGACTCTA
TCTGATGAA GGGCTTGGC CACTGCCACA GCACCTTGA TCGCGGGAC TGTGCGCC ACGTGTGGA GGGCCACAG GATGTCAGA GTCTGAGAT

177 D Y F P E P V T V S W N S G A L T S G V H T F P A V L Q S S G L Y

2201 CTCCTCAGC AGCGTGTGA CTGTGCCCTC TAGCAGCTTG GGCACCCAGA CCTACATCTG CAAGTGAAT CACAAGCCCA GCAACACCAA GGTGACAAAG
GAGGAGTCG TGCACCACT GACACGGAG ATCGTCGAAC CCGTGGTCT GATGTAGAC GTTGACTTA GTTGGGTG GTTGGGTG GTTGGGTG GTTGGGTG

210 S L S S V V T V P S S S L G T Q T Y I C N V N H K P S N T K V D K

2301 AAGTTGAGC CCAATCTTG TGACAAACT CACATGCC CACGTGCC AGCACTGAA CTCCTGGGG GACGTCAGT CTTCCTCTC CCCCCAAAAC
TTTCAACTCG GGTTAGAAC ACTGTTTGA GTGTGACGG GTGCGAGGG TCGTGACTT GAGACCCCC CTGGAGTCA GAAGGAGAG GGGGTTTTG

243 K V E P K S C D K T H T C P P C P A P E L L G G P S V F L F P P K P

2401 CCAAGGACAC CCTCATGATC TCCCGACCC CTGAGTCAAC ATGCGTGGT GTGGAGTGA GCCACGAAGA CCTGAGGTC AAGTCAACT GGTACGTGGA
GGTCTCTG GAGTACTAG AGGCGTGG GACTCCAGT TACGACCAAC CACTGCACT CGGTCTCTT GGTGCTTCTT TCAAGTTGA CCATGCACT

277 K D T L M I S R T P E V T C V V V D V S H E D P E V K F N W Y V D

FIG. 3B

METHODS AND COMPOSITIONS FOR INCREASING
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2501 CGCGGTGGAG GTGCATAATG CCAAGACAAA GCCGCGGGAG GAGCAGTACA ACAGCAGCTA CCCTGTGGTG AGCGTCCTCA CCGTCCTGCA CCAGGACTGG
GCCGCACCTC CACGTATTAC GGTCTGTGTT CGCGCCCTC CTCGTCATGT TGTGTGTCAT GGCACACCAG TCGCAGGAGT GGCAGGACGT GGTCTCTGACC
310 G V E V H N A K T K P R E E Q Y N S T Y R V V S V L T V L H Q D W
2601 CTGAATGGCA AGGAGTACAA GTGCAAGTTC TCACAAAG CCTCTCCAG CCCATCCAG AAACCATCT CCAAGGCCAA AGGCAGCCC CGAGAACCCAC
GACTTACGT TCCTCATGTT CAGGTTCCAG AGGTGTTTC GGGAGGTG GGGTAGCTC TTGTGTAGA GGTTCGGTT TCCGTCGGG GCTCTTGGTG
343 L N G K E Y K C K V S N K A L P A P I E K T I S K A K G Q P R E P Q
2701 AGGTGTACAC CTGCCCCCA TCCCGGAAG AGATGACAA GAACAGGTC AGCTGACT GCCTGTGCAA AGCTTCTAT CCCAGCGACA TCGCCGTGGA
TCCACATGTG GGACGGGGT AGGGCCCTTC TCTACTGTT TCTGTGTCAG TCGACTGGA CGACCACTGTT TCCGAAGATA GGTGCGCTGT AGCGCACCT
377 V Y T L P P S R E E M T K N Q V S L T C L V K G F Y P S D I A V E
2801 GTGGGAGAGC AATGGGCAGC CGGAGACAA CTACAAGACC AGCCTCCCG TCGTGGACTC CGACGGCTCC TTCTTCTCT ACAGCAAGCT CACGTGGAC
CACCTCTCG TTACCGGTG GCCTCTGTT GATGTTCTGG TCGGAGGGC ACGACCTGAG GCTGCCGAGG AAGAAGGAGA TGTGTTTCA GTGGCACCTG
410 W E S N G Q P E N N Y K T T P P V L D S D G S F F L Y S K L T V D
2901 AAGAGCAGGT GGCAGCAGG GAACTCTTC TCATGCTCCG TGATGCATGA GCTCTGCAC AACCACTACA CGCAGAAGAG CCTCTCCCTG TCTCCGGTA
TTCGTCCTCA CCGTGTCCC CTTCGAGAG AGTACGAGG ACTACTACT CCGACACGTG TTGTGTATGT GCGTCTCTC GGAGAGGAC AGAGGCCAT
443 K S R W Q G N V F S C S V M H E A L H N H Y T Q K S L S L S P G K
3001 AATAAGCATG CGACGGCCCT AGAGTCCCTA ACGTCTGGT CGCGCGGGC GTTTTTATT GTTAAGTCAT GTTTGACAGC TTATCATCGA TAAGCTTTAA
TTATTCGTAC GCTGCCGGA TCTCAGGAT TCCGAGCAA CGCGCGGCCG CAAAAATAA CAATTGAGTA CAACTGTCTG AATAGTAGCT ATTCGAAATT
477 O
3101 TCGGTAGTT TATCACAGTT AAATTGCTAA CGAGTCAGG CACGTGTAT GAATCTAAC AATGGCTCA TCGTCATCT CGGCACCGTC ACCCTGGATG
ACGCCATCAA ATAGTGTCAA TTACGATT CCGTCAGTCC GTGGCACATA CTTTAGATTG TTACCGAGT AGCAGTAGGA GCCGTGGCAG TGGGACCTAC
*Start Tet Resistance Coding Sequence
3201 CTGTAGGCAT AGGCTTGGTT ATGCCGGTAC TCCCGGGCCT CTTGCGGGAT ATCGTCCATT CCGACAGCAT CGCAGTCAC TATGGCGTC TGCTAGCGCT
GACATCCGTA TCCGAACCA TACGGCCATG ACGGCCCGA GAACGCCCTA TAGCAGGTAA GGCTGTGTA GCGGTGAGTG ATACCGCAGC ACGATCCGGA
3301

FIG. 3C

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1 GAATTCAACT TCTCCATACT TTGGATAAGG AATACAGAC ATGAAAATC TCATTGCTGA GTTGTTATTT AGGTTGGCC AAAAAGAAGA AGAGTCGAAT
CTTAAGTTGA AGAGGTATGA AACCTATTCC TTTATGCTCG TACTTTTAG AGTAACGACT CAACATAAA TTTCGAACGG TTTTCTTCT TCTCAGCTTA

101 GAACTGTGT GCGAGGTAGA AGCTTTGGAG ATTATCGTCA CTGCAATGCT TCGCAATATG GCGCAAAATG ACCAACAGCG GTTGATTGAT CAGGTAGAGG
CTTGACACAC GCGTCCATCT TCGAAACCTC TAATAGCAGT GAGTTACGA AGCTTATAC CCGTITTTAC TGGTTGTGCG CAACTAACCTA GTCCATCTCC

201 GGGCGCTGTA CGAGGTAAAG CCGGATGCCA GCATTCCTGA CGACGATACG GAGCTGTGCG GCGATTACGT AAAGAAGTTA TTGAAGCATC CTGTCAGTA
CCCGGACAT GCTCCATTTC GGGCTACGCT CGTAAGGACT GTGTCTATGC CTGACGACG CGCTAATGCA TTTCTTCAAT AACTTCGTAG GAGCAGTCAT

301 AAAAGTTAAT CTTTCAACA GCTGTCAATA AGTTGTACG GCGGACCTT ATAGTCGCTT TGTTTTAT TTTTAATGTA TTTGAACCTA GTACGCAAGT
TTTTCATTA GAAAGTTGT CGACAGTATT TCAACAGTGC CCGCTCTGAA TATCAGCGAA ACAAAATAA AAAATTACAT AACATTGAT CATGCGTTCA

401 TCACGTAAAA AGGTATCTA GAATTATGAA GAAGAATATC GCATTTCTTC TTGCATCTAT GTTCGTTTT TCTATTGCTA CAAACGCTA CGCTGATATC
AGTGCATTTT TCCCATAGAT CTTAATACCT CTTCTTATAG CGTAAGAAG AACGTAGATA CAAGCAAAA AGATAACGAT GTTTCGCGAT GCGACTATAG

1 M K K N I A F L L A S M F V F S I A T N A Y A D I
^STII signal TIR -1 ^light chain

501 CAGTTGACCC AGTCCCGGAG CTCCCTGTCC GCCTCTGTGG GCGATAGGT CACCATCACC TGCAGCGCAA GTCCAGGATAT TAGCAACTAT TTAACTGGT
GTCAACTGGG TCAGGGGCTC GAGGGACAGG CGGTATCCCA GTGTAGTGG ACCTGCGCTT CAGTCCCTATA ATCGTTGATA AATTGACCA

26 Q L T Q S P S S L S A S V G D R V T I T C S A S Q D I S N Y L N W Y

601 ATCAACAGAA ACCAGSAAA GCTCCGAAAG TACTGATTTA CTTACCTCC TCTCTCACT CTGGAGTCCC TTCTGCTTC TCTGGATCCG GTTCTGGAC
TAGTTGTCTT TGGTCCCTTT CGAGGCTTTC ATGACTAAAT GAAGTGGAGG AGAGAGTGA GACCTCAGG AAGAGCGAAG AGACCTAGGC CAAGACCCCTG

60 Q Q K P G K A P K V L I Y F T S S L H S G V P S R F S G S G S G T

701 GGATTTCACT CTGACCATCA GCAGTCTGCA GCCAGAAGAC TTCGCAACTT ATTACTGCTA ACAGTATAGC ACCGTGCCGT GGAGTTTGG ACAGGGTACC
CCTAAAGTGA GACTGGTAGT CGTCAGACGT CCGTCTTCTG AAGCGTTGAA TAATGACAGT TGTATATCG TGGCAGCGCA CCTGCAAAACC TGTCCCATGG

93 D F T L T I S S L Q P E D F A T Y Y C Q Q Y S T V P W T F G Q G T

801 AAGGTGGAGA TCAACGAAAC TGTGGCTGCA CCATCTGTCT TCATCTTCCC GCATCTGAT GAGCAGTTGA AATCTGAAAC TGTCTCTGTT GTGTGCTGC
TTCCACCTCT AGTTTGCTTG ACACCGACGT GGTAGACAGA AGTAGAAGG CGGTAGACTA CTCGTCACCT TTAGACCTTG ACGAAGACAA CACACGGACG

126 K V E I K R T V A A P S V F I F P P S D E Q L K S G T A S V V C L L

901 TGAATAACTT CTATCCAGA GAGGCCAAAG TACAGTGGAA GGTGGATAAC GGCCTCCAAT CCGGTAACCTC CCAGGAGAGT GTCACAGAGC AGGACAGCAA
ACTTATTGAA GATAGGTCT CTCCGTTTC ATGTCACCTT CCACCTATTG CCGGAGTTA GCCCATGAG GTCCCTCTCA CAGTGTCTCG TCCTGTGCTT

160 N N F Y P R E A K V Q W K V D N A L Q S G N S Q E S V T E Q D S K

1001 GGACAGCAC TACAGCCTCA GCAGCACCTT GAGCCTGAGC AAGCAGACT ACGAGAAACA CAAAGTCTAC GCTTGGGAG TCACCCATCA GGGCCTGAGC
CCTGTCGTGG ATGTCGAGT CGTCGTGGGA TTTGCTCTGA TGTCTTTGT GTTTCAGATG CCGACGCTTC AGTGGGTAGT CCCGGACTCG

193 D S T Y S L S S T L T L S K A D Y E K H K V Y A C E V T H Q G L S

FIG. 4A

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1001 GGACAGCACC TACAGCCTCA GCAGCACCCCT GACGCTGAGC AAGCAGACT ACGAGAACA CAAGTCTAC GCCTGGGAAG TCACCCATCA GGGCCTGAGC
CCTGCTGG AGTTCGGAGT CGTCTGGGA CTGCGACTCG TTTCGTCTGA TGCTCTTGT GTTTCAGATG CGGACGCTTC AGTGGGTAGT CCGGACTCG
193 D S T Y S L S S T L T L S K A D Y E K H K V Y A C E V T H Q G L S
1101 TCGCCCGTCA CAAAGAGCTT CAACAGGGGA GAGTGTAAAT TAAATCCTCT ACGCCGGACG CATCGTGSCG AGCTCGGTAC CCGGGGATCT AGGCCTAACG
AGCGGGCAGT GTTTCGAA GTTTCGCCCT CTCACAAATTA ATTAGGAGA TCGCGCTGC GTAGCACCGC TCGAGCCATG GGGCCCTAGA TCGGATTCG
226 S P V T K S F N R G E C O
lambda t0 terminator
1201 CTCGGTTGCC GCGGGCGTT TTTTATTGTT GCCGACGCG ATCTCGAATG AACTGTGTGC GCAGGTAGAA GCTTTGGAGA TTATCGTCAC TGCAATGCTT
GAGCCAAACG CGGCCGCGAA AAAATAACAA CGGCTGCGG TAGAGCTTAC TTGACACACG CGTCCATCTT CGAAACCTCT AATAGCAGT ACCTTACGAA
1301 CGCAATATGG CGCAAAATGA CCAACAGCGG TTGATTGATC AGGTAGAGG GGGCTGTATC GAGGTAAAGC CCGATGCCAG CATTCTGAC GACGATACGG
GGTTATACC GCGTTTACT GGTGTGCGC AACTAACTAG TCCATCTCCC CCGGACATG CTCCATTCG GGTACGGTC GTAAGGACTG CTGCTATGCC
1401 AGCTGCTGCG CGATTACGTA AAGAAGTTAT TGAAGCATCC TCGTCAGTAA AAGTTAATC TTTTCAACAG CTGTCAATAA GTTGTACCG CCGAGACTTA
TCGACGACG GCTAAATGCAT TTCTTCAATA ACTTCGTAGG AGCAGTCAT TTTCAATTAG AAAAGTTGTC GACAGTATT CAACAGTGCC GGCTCTGAAT
1501 TAGTCGCTTT GTTTTATT TTAAATGAT TTGTAACATG TAGGCAAGTT CACGTAAATA GGGTATCTAG AATTATGAG AAGAATATCG CATTCTCTCT
ATCAGCGAA CAAAATAAA AATTATGATC ATGCGTTCAA GTGCAATTTT CCCATAGATC TTAATCTTC TTCTTATAGC GTAAAGAAGA
M K K N I A F L L
*STII Signal TIR-1
1601 TGCATCTATG TTGTTTTTTT CTATTGCTAC AAACGCGPAC GGTAGGTTG AGCTGTGGA GTCTGGCGGT GGCCTGTGTC AGCCAGGGG CTCACCTCGT
ACGTGATAC AAGCAAAATA GATACGATG TTTCGCGATG CGACTCCAAG TCACCACTT CAGACGCGCA CCGGACACG TCGTCTCCCC GAGTGAGCA
10 A S M F V F S I A T N A Y A E V Q L V E S G G L V Q P G G S L R
*start heavy chain
1701 TTGCTCTG CAGCTTCTGG CTATACCTTC ACCAATATG GTATAAATG GGTCTGCTAG GCCCGGGTA AGGGCTTGA ATGGTTTGA TGGATTAAACA
AACAGGACAC GTCAAGACC GATATGGAAG TGTTGATAC CATATTGAC CCAGGACATC CGGGGCCCAT TCCCGACCT TACCCAACT ACCTAATGT
43 L S C A A S G Y T F T N Y G I N W V R Q A P G K G L E W V G W I N T
1801 CCTATACCG TGAACCGACC TATGCTGCG ATTTCRAAG TCGTTTCACT TTTTCTTTAG ACACCTCAA AAGCAGCA TACTGCAGA TGAACAGCCT
GGATATGCC ACTTGGCTG ATACAGCGC TAAAGTTGC AGCAAGTGA AAAAGAAATC TGTGAGGT TTCTGTCTCG ATGACGCTCT ACTTGTGGA
77 Y T G E P T Y A A D F K R R F T F S L D T S K S T A Y L Q M N S L
1901 GCGCGCTGAG GACACTGCG TCTATTACTG TGAAGATAC CCGCACTATT ATGTGAACGA GCGGAAGAGC CACTGGTATT TCGACGCTG GGTCAAGGA
CGCGGACTC CTGTGAGGC AGATAATGAC AGTTTTCATG GGCCTGATAA TACACTTGT CGCTTCTCG GTGACCAATA AGCTGCAGAC CCCAGTTCT
110 R A E D T A V Y Y C A K Y P H Y Y V N E R K S H W Y F D V W G Q G
2001 ACCTGTGTC CCGTCTCTC GGCCTCCACC AAGGGCCCAT CGTCTTCCC CCGTCCACCC TCCTCCAGA GCACCTCTGG GSGCACAGC GCCCTGGCT
TGGACCACT GGCAGAGG CCGGAGGTG TTCCCGGTA GCCAAGGG GACCGTGG AGGAGTTCT CGTGAGACC CCGTGTGCG CGGACCCGA
143 T L V T V S S A S T K G P S V F P L A P S S K S T S G G T A A L G C
2101 GCTGTGTC GACTACTC CCGAACCG TGACGTGTC GTGAATCA GCGCCCTGA CCAAGCGGT GCACACTTC CCGGCTGTCC TACAGTCTC
CGGACAGTT CCTGATGAG GGGCTTGCC ACTGCCACAG CACTTGATG CCGGGGACT GGTGCGCGA CGTGTGAAG GCGGACAG ATGTGAGG
177 L V K D Y F P E P V T V S W N S G A L T S G V H T F P A V L Q S S

FIG. 4B

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2101 GCCTGGTCAA GGAAGTCTTC CCGAACCAGG TGACGGTGTG GTGAAGTCA GCGCCCTGTA CCACGGCGGT GCACACCTTC CCGGCTGTCC TACAGTCTTC
CGGACCAAGT CCTGATGAAG GGGCTTGGCC ACTGCCACAG CACTTGAGT CCGGGGACT GGTGCGCGCA CGTGTGAAG GCGCGACAGG ATGTCAGGAG
177 L V K D Y F P E P V T V S W N S G A L T S G V H T F P A V L Q S S
2201 AGGACTTAC TCCCTCAGCA GCGTGGTGAC TGTGCCCTCT AGCAGCTTGG GCACCCAGAC CTACATCTGC AACGTGAATC ACAAGCCAG CAACACCAAG
TCTTGAGATG AGGAGTCTCG CGCACCACTG ACACGGGAGA TCGTCGAACC CGTGGTCTG GATGTAGACG TTGCACTTAG TGTTCGGGTC GTTGTGGTTC
210 G L Y S L S S V V T V P S S S L G T Q T Y I C N V N H K P S N T K
2301 GTGACACAGA AAGTTGAGCC CAATCTTGT GACAAACTC ACATGCCC ACCGTGCCA GCACCTGAAC TCCTGGGGG ACCGTCAATC TTCCTCTTCC
CACTGTCTT TCAACTCGG GTTTAGAACA CTGTTTGG TGTGTACGG TGGCAGGGT CGTGGACTG AGGACCCCC TGGCAGTCAG AAGGAGAAG
243 V D K K V E P K S C D K T H T C P P C P A P E L L G G P S V F L F P
2401 CCCCACCAACC CAAGGACACC CTCATGATCT CCGGACCCC TGAGTCACTA TGGTGGTGG TGGACGTGAG CCACGAAGAC CCTGAGGTCA AGTTCAACTG
GGGTTTGG GTTCTGTGG GAGTACTAGA GGGCTTGGG ACTCCAGTGT AGCACCAACC ACTGCACTC GGTGTTCTG GACTCCAGT TCAAGTTGAC
277 P K P K D T L M I S R T P E V T C V V D V S H E D P E V K F N W
2501 GTAGTGGAC GGCCTGGAGG TGCATAATGC CAAGACAAAG CCGGGGAGG AGCAGTACAA CAGCAGGTAC CGTGTGTCA GGTCTCTCAC CGTCTGCAC
CATGCACTG CCGCACTCC ACATATTAG GTTCTGTTT GCGGCCCTCC TCGTCATGTT GTGTGATG GCACACCACT CCGCAGAGTG GCAGGACGTG
310 Y V D G V E V H N A K T K P R E E Q Y N S T Y R V V S V L T V L H
2601 CAGGACTGGC TGAATGGCAA GGAGTACAA TGCAAGTCT CCAACAAGC CCTCCAGCC CCATCGAGA AACCATCTC CAAAGCCAA GGCAGGCCCC
GTCTGACCG ACTTACCGTT CCTCATGTC ACCTTCCAGA GGTGTTTCG GGAGGTTCG GGTGATCTT TTTGGTAG GTTTCGTTT CCGTCGGG
343 Q D W L N G K E Y K C K V S N K A L P A P I E K T I S K A K G Q P R
2701 GAGAACACA GGTGTACCC CTGCCCCAT CCGGGAAGA GATGACCAAG AACCAAGTCA GCTGACCTG CCTGGTCAA GGTCTTATC CCAGCGACAT
CTCTTGGTGT CCACATGTT GACGGGGTA GGGCCCTTCT CTACTGTTT TGTGTCAGT CCGACTGGAC GGACCAAGT CCGAAGATAG GGTGCTGTA
377 E P Q V Y T L P P S R E E M T K N Q V S L T C L V K G F Y P S D I
2801 CCGCTGGAG TGGGAGACA ATGGGACGCC GGAGAACAC TACAAGACA CCGCTCCGT GCTGGACTCC GACGGTCTCT TCTTCTCTA CAGCAAGCTC
GGGGACCTC ACCCTCTCT TACCGTCCG CCTCTTGTG CTCTTGTG GCGAGGGCA CAGCTGAGG CTGCGGAGGA AGAAGGAGAT GTGCTTCGAG
410 A V E W E S N G Q P E N N Y K T T P P V L D S D G S F F L Y S K L
2901 ACCGTGGACA AGACAGGTG GCAGCAGGG AACGTCTTCT CATGCTCCGT GATCATGAG GCTCTGACA ACCACTACAC GCAGAAGAGC CTCTCCCTGT
TGGCACTGT TCTGTCAC CGTCGTCCC CGTCGTCCC TTGCAAGA GATGAGGCA CTAGTACTC CGAGAGGTGT TGGTGTGTG CGTCTTCTG GAGAGGACA
443 T V D K S R W Q Q G N V F S C S V M H E A L H N H Y T Q K S L S L S
3001 CTCGGGTAA ATAGCATGC GACGGCCCTA GAGTCCCTAA CGCTCGGTTG CCGCGGGGG TTTTATTG TTAATCATG TTTGACAGT TATCATCAT
GAGGCCATT TATTCGTAG CTGCGGGAT CTCAGGGATT GCGAGCAAC GCGGCCCGC AAAAAATAAC AATTGATAC AAATGTGCA ATAGTAGCTA
477 P G K O
^lambda terminator
3101 AAGCTTTAAT CCGTAGTATT ATCAGATTA AATTGCTAAC GCAGTCAGGC ACGGTGTATG AAATCAACA ATGCGTCTAT CGTCATCTC GGCACCGTCA
TTGGAATTA CGCATCAA TAGTGTAAT TTAAGATTG CGTACGCG TGGACATAC TTTAGATTG TACGCGAGTA GCAGTAGGAG CCGTGGCAGT
3201 CCTGGATGC TGTAGGCATA GGCTTGGTTA TGCCGGTACT GCGGGCCTC TTGGG
GGGACCTACG ACATCCGTAT CCGAACCAAT ACGGCCATGA CCGCCGGAG AACGC

FIG. 4C

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3201 CCTTGGATGC TGTAGGATA GGCTTGGTTA TGCCGGTACT GCCGGCCTC TTGCG
GGGACCTAG ACATCCGTAT CCGAACCAAT ACGGCCATGA CGGCCCGGAG AACGC

FIG. 4D

METHODS AND COMPOSITIONS FOR INCREASING
ANTIBODY PRODUCTION

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1 ATCGATGAAT TCATGCTGTG GTGTCAATGGT CCGTGATCGC CAGGGTGCCG ACGGCATCT CGACTGCAAG GTGCACCAAT GCTTCTGGCG TCAGGCAGCC
TAGCTACTTA AGTACGACAC CACAGTACCA GCCACTAGCG GTCCACGGC TCGCGGTAGA GCTGACGTG CAGGTGGTTA CGAAGACCGC AGTCCGTCGG
^ClaI

101 ATCGGAAGCT GTGGTATGGC TGTGCAGGTC GTAATCACT GCATAATTCG TGTGCTCAA GCGGCACTCC CGTCTGGAT AATGTTTTT GCGCCGACAT
TAGCCTTCGA CACCATACCG ACAGGTCCAG CATTTAGTGA CGTATTAGC ACAGGAGTT CCGCGTAGG GCAAGACCTA TTACAAAAA CGCGGCTGTA

201 CATPAACGGT CTGGCAAATA TTCTGAATG AGCTGTGAC AATTAATCAT CGAACTAGTT TAATGTGTG AATGTGTGAC GGATAACAAT TAAGCTTAGG
GTATTGCCAA GACCGTTTAT AAGACTTTAC TCGACAACTG TTAATTAGTA GCTTGATCMA ATTACACACC TTAACACTCG CCTATTGTTA ATTGGAATCC

301 ATTCTAGAGG GAAAGATTAT GAAATCACTG TTAAAGTAA CGCTGTGGC GACCACAATG GCGGTGCCC TGCATGCACC AATCACTTTT GCTGCTGAAG
TAAGATCTCC CTTCTAAATA CTTTAGTGAC AAATTTCAIT GCGACGACCG CTGGTGTAC CGGCAACGGG ACGTACGTGG TTAGTGAAAA CGAGCACTTC
1 M K S L F K V T L L A T T M A V A L H A P I T F A A E A
^EkpA start

401 CTGCAAAACC TGCTACAGCT GCTACAGCA AAGCAGGTT CAAAATGAC GATCAGAAT CAGCTTATGC ACTGGTGCC TCGCTGGGTC GTTACATGGA
GAGTTTTGG ACGATGTGCA CGACTGTGCT TTGCTGGCAA GTTTTACTG CTAGTCTTTA GTCGAATACG TGACCCACGG AGCGACCCAG CAATGTACCT
29 A K P A T A A D S K A A F K N D D Q K S A Y A L G A S L G R Y M E

501 AACTCTCTA AAAGAACAG AAAAAGCTGG CATCAAACTG GATAAGATC AGCTGATCG TGGTGTTCAG GATGCAITTG CTGATAAGAG CAAACTCTCC
TTTGAGAGAT TTCTGTTC TTTTGAACC GTAGTTTGAC CTATTTCTAG TCGACTAGCG ACCACAAGTC CTAGGTAAAC GACTATCTC GTTTGAGAGG
62 N S L K E Q E K L G I K L D K D Q L I A G V Q D A F A D K S K L S

601 GACCAAGAGA TCGAACAGAC TCTACAAGCA TTGGAAGCTC GCGTGAATC TTCTGTCTAG GCGAAGATGG AAAAAGACGC GGCTGATAAC GAAGCAAAAG
CTGGTCTCT AGCTGTCTG AGATGTTCTG AAGCTTCGAG CGCACTTCAG AAGACGAGTC CGCTTCTACC TTTTCTGCG CCGACTATTG CTTCTGTTTC
95 D Q E I E Q T L Q A F E A R V K S S A Q A K M E K D A A D N E A K G

701 GTAAAGAGTA CCGCGAGAAA TTGCGCAAG AGAAGGTGT GAAACCTCT TCAACTGTC TGGTTTATCA GGTAGTAGAA GCGGTAAAG GCGAAGCACC
CAATTTCTCAT GCGGCTCTTT AAAGGTTTC TCTTTCCACA CTTTGGAGA AGTTGACAG ACCAATAGT CCATCATCTT CGGCCATTT CCGTTCGTGG
129 K E Y R E K F A K E K G V K T S S T G L V Y Q V V E A G K G E A P

801 GAAAGACAGC GATCTGTTG TAGTGAATA CAAAGGTACG CTGATCGACG GTAAAGAGTT CGACAATCT TACACCCGTG GTGAACCGCT TTCTTTCGGT
CTTCTGTGCT CTATGACAAC ATCACTTGAT GTTTCATGC GACTAGTGC CATTTCTCAA GCTGTTGAGA ATGTTGGCAC CACTTGGCGA AAGAAAGGCA
162 K D S D T V V V N Y K G T L I D G K E F D N S Y T R G E P L S F R

901 CTGGACGGTG TTATCCGGG TTGGACAGAA GGTCTGAAGA ACATCAGAA AGGCGGTAAG ATCAACTGG TTATTCACC AGAATGGCT TACGGCAAG
GACCTGCCAC AATAGGCC CAACTGTCTT CCAGACTTCT TGTAGTCTT TCCGCCATTC TAGTTGACC AATAAGGTGG TCTTGACCGA ATGCCGTTTC
195 L D G V I P G W T E G L K N I K K G G K I K L V I P P E L A Y G K A

FIG. 5A

1001 CGGGTGTTC GGGATCCCA CCGAATTCTA CCTGTGTGT TGACGTAGAG CTGCTGGATG TGAACACAGC GCCGAAGGCT GATGCAAAGC CGGAAGCTGA
GCCACACAAG CCCCTAGGGT GGCTTAAGAT GGGACCACAA ACTGCACTTC GACGACCTAC ACTTTGGTCG CGGCTTCGGA CTACGTTTCG GCCTTCGACT
229 G V P G I P P N S T L V F D V E L L D V K P A P K A D A K P E A D
1101 TGGCAAAGCC GCAGATTCTG CTAAAAAATA AAAGCTAGC
ACGCTTTCGG CGTCTAAGAC GATTTTAT TTTGATCG
262 A K A A D S A K K O ^NheI

FIG. 5B

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1 GAATTCAACT TCCTCATACT TTGGATAAGG AAATACAGAC ATGAAAAATC TCATTGCTGA GTTGTATTATTT AAGCTTGCCC AAAAAAGA AGAGTCGAAT
CTTAAGTTGA AGAGGTATGA AACCTATTCC TTTATGCTG TACTTTTATG AGTAACGACT CAACAATAAA TTCGAACGGG TTTTCTCTCT TCTCAGCTTA
^EcoRI

101 GAACGTGTG CGCAGGTAGA AGCTTTGGAG ATTATCTGCA CTGCAATGCT TCGCAATATG GCGCAAAATG ACCAACAGCG GTTGATTGAT CAGGTAGAGG
CTTGACACAC GCGTCCATCT TCGAAACCTC TAATAGCAGT GACGTTACGA ACGGTTATAC CGCGTTTAC TGGTTGTCGC CAACTAACTA GTCCATCTCC

201 GGGCGCTGTA CGAGGTAAAG CCCGATGCCA GCATTCTCTGA CGACGATAG GAGCTGCTGC GCGATTACGT AAAGAAGTTA TTGAAGCATC CTGCTCAGTA
CCCGGACAT GCTCCATTTC GGGCTACGGT CGTAAGGACT GCTGCTATGC CTCGACGACG CGCTAATGCA TTTCTTCAAT AACTTCGTAG GAGCAGTCAT

301 AAAAGTTAAT CTTTTCACCA GCTGTCATAA AGTTGTCAAG GCGGAGACTT ATAGTCGCTT TGTTTTATTT TTTTAATGTA TTTGTAAC TAACGCAAGT
TTTTCAATTA GAAAAGTTGT CGACAGTATT TCAACAGTGC CGGCTCTGAA TATCAGCGAA ACAAAAATAA AAAATTACAT AAACATTGAT CATGCGTTCA

401 TCACGTAAAA AGGTATCTA GAATTATGAA AAAGAATATC GCATTCTTC TTGATCTAT GTTCGTTTTT TCTATTGCTA CAAACGCGTA CGCTGATATC
AGTGCATTTT TCCCATAGAT CTTAATACCT TTTCTTATAG CGTAAAGAG AACGTAGATA CAAGCAAAA AGATAACGAT GTTTCGCGAT CGCATATAG
M K K N I A F L L A S M F V F S I A T N A Y A D I
^start SII signal TIR 7 anti-TF light chain^

501 CAGATGACCC AGTCCCGAG CTCCTCTGCC GCCTCTGCG GCGATAGGT CACCATCACC TGCAGAGCCA GTCCGACAT CAAAGAGCTAT CTGAAGTGT
GTCTACTGG TCAGGGGCTC GAGGACAGG CGGAGACACC CGCTATCCCA GTGGTAGTGG ACGTCTCGGT CAGCGTGA GTTCTCGATA GACTTGACCA
26 Q M T Q S P S S L S A S V G D R V T I T C R A S R D I K S Y L N W Y

60 Q Q K P G K A P K V L I Y Y A T S L A E G V P S R F S G S G T

701 GGATTACACT CTGACCATCA GCAGTCTGCA GCCAGAGAC TTCGCAACTT ATTACTGTCT TCAGCACGGA GAGTCTCCAT GGCATTGG ACAGGTACC
CCTAATGTA GACTGGTAGT CGTCAGACGT CGGTCTCTCTG AAGGTTGAA TAATGACAGA AGTCTGCTCT CTCAGAGGTA CCTGTAACCC TGTCCTATGG
93 D Y T L T I S S L Q P E D F A T Y Y C L Q H G E S P W T F G Q G T

801 AAGGTGGAGA TCAACGAAC TGTGGCTGCA CCATCTGTCT TCATCTTCCC GCCATCTGAT GAGCAGTTGA AATCTGGAAC TGCTTCTGTT GTGTGCTGC
TTCCACCTCT AGTTTGCTTG ACACCGACGT GGTAGACAGA AGTAGAAGGG CGGTAGACTA CTGCTCACT TTAGACCTTG ACGAAGACAA CACAGGACG
126 K V E I K R T V A A P S V F I F P P S D E Q L K S G T A S V V C L L

901 TGAATAACTT CTATCCAGA GAGGCCAAAG TACAGTGGAA GGTGATAAC GCCCTCCAAT CCGGTAACCTC CCAGGAGAGT GTCACAGAGC AGGACAGCAA
ACTTATTGAA GATAGGTCT CTCCGGTTTC ATGTACCTT CCACCTATG CCGGAGGTTA GCCCATGAG GGTCTCTCA CAGTGTCTCG TCCTGTCTGTT
160 N N F Y P R E A K V Q W K V D N A L Q S G N S Q E S V T E Q D S K

FIG. 6A

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1001 GGACAGCACC TACAGCCTCA GCAGCACCCCT GACGCTGAGC AAGCAGACT ACGAGAAACA CAAAGTCTAC GCCTGCGAAG TCACCCATCA GGGCCTGAGC
CCTGTGCTGG ATGTCGAGT CGTGTGAGG CTGCGACTCG TTCTGCTGA TGTCTTTGT GTTTCAGATG CCGAGCTTC AGTGGGTAGT CCCGACTCG
193 D S T Y S L S S T L T L S K A D Y E K H K V Y A C E V T H Q G L S
1101 TCGCCCGTCA CAAAGAGCTT CAACAGGGGA GAGTGTAAAT TAAATCTCTT ACGCCGAGC CATCGTGGG AGCTCGGTAC CCGGGGATCT AGGCCTAACG
AGCGGCGAGT GTTCTCGAA GTTGTCCTCT CACCAATTA ATTAGGAGA TCGCGCTGCG GTAGCACCGC TCGAGCCATG GCGCCCTAGA TCCGGATTGC
226 S P V T K S F N R G E C O
lambda t0 terminator^{*}
1201 CTCGGTTGCC GCGGGCGTT TTTTATTGTT GCGGACGCG ATCTGCGTG CACGGTGCAC CAATGCTTCT GCGTCAAGC AGCATCGGA AGCTGTGGTA
GAGCCAACCG CCGCCCGCAA AAAATAACAA CCGCTGCGCG TAGAGCTGAC GTGCCAGTG GTTAGCAAGA CCGCAGTCCG TCGGTAGCCT TCGACACCAT
1301 TGGGTGTGCA GGTGTAAT CACTGCATAA TTCTGTGCG TCAAGGCGA CTCCCGTCT GGATAATGTT TTTTGGCGG ACATCATAAC GGTTCCTGGCA
ACCGACACGT CCAGCATTTA GTGACGTATT AAGCACAGCG AGTTCCGCGT GAGGGCAAGA CCTATTACAA AAAACGCGG TGTAGTATTG CCAAGACCGT
1401 AATATTCTGA AATGAGCTGT TGACAATTAA TCATCGAACT AGTTTAATGT GTGGAATGT GAGCGGATAA CAATTAAGCT TAGGATCTAG AATTATGAAG
TTATAAGACT TTAGTCGACA ACTGTAAAT AGTAGCTTGA TCAATTACA CACCTTAACA CTCGCCTATT GTTAATCGA ATCCTAGATC TTAATPACTT
M K
1 Start STII signal TIR 3^{*}
1501 AAGAATATTG CGTTCCTACT TGCCTCTATG TTTGCTCTTT CTATAGCTAC AAACGGGTAC GCTGAGTTC AGCTGGTGA GTCTGGCGGT GGCCTGGTGC
TTCTTATAAC GCAGGATGA ACGGAGATAC AAACAGAAA GATATCGATG TTTGCGATG CGACTCCAG TCGACACCT CAGACCCCA CCGGACCAAG
3 K N I A F L L A S M F V F S I A T N A Y A E V Q L V E S G G L V Q
^anti-TF heavy chain
1601 AGCCAGGGG CTCACTCGT TGTCTCTGT CAGCTCTG CAGCTCTG AAGGAGTACT ACATGCACTG GGTCTGCTAG GCCCGGGTA AGGCCTGGA
TCGGTCCCGG GAGTGAGCA AACAGGACAC GTCCAGACCC GAAGTATTA TTTCTCATGA TGTACGTGAC CCAGGAGTC CCGGGCCCAT TCCCGGACCT
37 P G G S L R L S C A A S G F N I K E Y Y M H W V R Q A P G K G L E
1701 ATGGTTTGA TTGATTGATC CAGAGCAAG CACACAGATC TATGACCCGA AGTTCCAGGA CCGTGCCACT ATAAGGCTG ACAATTCCAA AAACAGCA
TACCAACCT AACTAAGTAG GTCTCGTTCC GTTGTGCTAG ATACTGGCT TCAAGTCTT GGCAGGCTGA TATTCGCGAC TGTAAAGTT TTTGTGCTGT
70 W V G L I D P E Q G N T I Y D P K F Q D R A T I S A D N S K N T A
1801 TACCTGCAGA TGAACAGCCT GGTGCTGAG GACACTGCGG TCTATTATTG TGTCTGAGC ACGCGCGCTT ACTTCGACTA CTGGGGTCAA GGAACCTGG
ATGGAGTCT ACTTGTGGA CGCAGACTC CTGTGACGCG AGATAATAAC ACGAGTCTG TCGCGCGGAA TGAAGCTGAT GACCCAGTT CTTTGGGACC
103 Y L Q M N S L R A E D T A V Y Y C A R D T A A Y F D Y W G Q G T L V
1901 TCACGCTCT CTCGGCTCC ACCAAGGCC CATCGTCTT CCGCTGGA CCGTCTTCCA AGACACCTC TGGGGSCACA GCGGCCCTGG GCTGCTGCT
AGTGCAGAG GAGCCGAGG TGGTCCCGG GTAGCCAGAA GGGGACCGT GAGGAGAGT TCTGTGAG ACCCGCTGT CCGCGGACC CGACGACCA
137 T V S S A S T K G P S V F P L A P S S K S T S G G T A A L G C L V
^ApaI
2001 CAAGGACTAC TTCCCGGAAC CCGTGACGCT GTCTGGAAC TCAGCGGCC TGACACAGCG GTGCACACC TTCCCGGCTG TCCTACAGTC CTCAGACTC
GTTCTGATG AAGGGGCTTG GCCACTGCA CAGCACTTG AGTCCGCGG ACTGTGCTCC GCAGTGTGG AAGGGCGGAC AGGATGTGAG GAGTCTGAG
170 K D Y F P E P V T V S W N S G A L T S G V H T F P A V L Q S S G L

FIG. 6B

2101 TACTCCTCTA GCAGCGTGGT GACTGTGCC TCTAGCAGCT TGGGACCCA GACCTACATC TGCAACGTGA ATCACAAGCC CAGCAACACC AAGGTGGACA
ATAGGGAGT CGTCGCACCA CTGACACGGG AGATCGTGA ACCCGTGGT CTGGATGTAG ACGTGCACT TAGTGTGG GTCTTTGG TTCACCTGT
203 Y S L S S V V T V P S S S L G T Q T Y I C N V N H K P S N T K V D K
2201 AGAAAGTTGA GCCCAAATCT TGTGACAAA CTCACACATG CCCACGTGC CCAGCACTG AACTCTCTGG GGGACCGTCA GTCTTCTCT TCCCCCAAA
TCTTTCAACT CGGTTTGA ACACTGTTT GAGTGTGTAC GGGTGGCAG GGTCTGTGAC TTGAGGACCC CCCTGGCAGT CAGAAGGAGA AGGGGGTTT
237 K V E P K S C D K T H T C P P C P A P E L L G G P S V F L F P P K
2301 ACCCAAGGAC ACCCTCATGA TCTCCGGAC CCTTGAAGTC ACATGGTGG TGTGTGAGT GAGCCAGAA GACCTGTAGG TCAAGTTCAA CTGGTACGTG
TGGTTCCTG TGGAGTACT AGAGGCGCTG GGAATCCAG TGTACGCACC ACCACCTGCA CTCGGTGTCTT CTGGGACTCC AGTTCAAGTT GACCATGCAC
270 P K D T L M I S R T P E V T C V V V D V S H E D P E V K F N W Y V
2401 GACGGCGTGG AGGTGCATAA TGCCAAAGACA AAGCCGCGG AGGAGAGTA CAACAGCAG TACCGTGTGG TCAGCGTCTCT CACCGTCTCT CACCAAGACT
CTGCCGACC TCCAGGTATT ACGTTCCTGT TTCCGGCGCC TCCTCGTCAT GTTGTCTGTC ATGGCACACC AGTCGCAGGA GTGGCAGGAC GTGGTCTCTGA
303 D G V E V H N A K T K P R E E Q Y N S T Y R V V S V L T V L H Q D W
2501 GGCTGAATGG CAAGGAGTAC AAGTGAAGG TCTCCAACAA AGCCCTCCCA GCCCCCATCG AGAAACCAT CTCCAAGCC AAAGGGCAGC CCGGAGAAC
CCGACTTACC GTTCTCATG TTCAGGTCC AGAGTTGTT TCGGGAGGT CGGGGTAGC TCTTTGTA GAGTTTCGG TTTCCTCTCG GGGCTCTGG
337 L N G K E Y K C K V S N K A L P A P I E K T I S K A K G Q P R E P
2601 ACAGGTGTAC ACCCTGCCCC CATCCGGGA AGAGATGACC AAGAACCAG TCAGCTGTAC CTGCTGTGTC AAAGGTTCT ATCCAGCA CATCGCGGTG
TGTCCACATG TGGACGGGG GTAGGGCCCT TCTCTACTGG TTCTTGGTCC AGTCGGACTG GACGACCAAG TTTCGGAAGA TAGGTCTGCT GTAGCGGCAC
370 Q V Y T L P P S R E E M T K N Q V S L T C L V K G F Y P S D I A V
2701 GAGTGGAGA GCAATGGGA GCGGAGAAC AACTACAAGA CCACGCTCC CGTGTGAGC TCCGACGGCT CCTTCTCTCT CTACAGCAAG CTCACCGTGG
CTCACCTCT CGTTACCCGT CGGCTCTTG TTGATGTTCT GGTGCGAGG GCAGCACTG AGGCTGCCGA GGAAGRAGGA GATGCTGTTT GAGTGCACCC
403 E W E S N G Q P E N N Y K T T P P V L D S D G S F F L Y S K L T V D
2801 ACAAGACAG GTGGCAGCAG GGAACGTCT TCTCATGCTC CGTGTGCTAT GAGGCTGTGC ACAACCACTA CAGCAGAAG AGCCTCTCC TGTCTCCGGG
TGTCTCTGTC CACCGTCTC CCCTTGCGA AGATPACGAG GCACTAGTA CTCGAGACG TGTGTGTAT GTGCTGTTT TCGGAGAGGG ACAGAGGCC
437 K S R W Q Q G N V F S C S V M H E A L H N H Y T Q K S L S L S P G
2901 TAAATAGCA TGGGACGGC CTAGAGTCCC TAAGCTCGG TTGCGCGCGG GCGTTTTTA TTGTTAACTC ATGTTTGACA GCTTATCATC GATAAGCTTT
ATTATTCGT ACGTGCCTG GATCTCAGG ATTGCGAGC AAGCGCGGCC CGCAAAAAAT AACAACTGT TACAATGAG CGAATAGTAG CTATTGAAA
470 K O
3001

FIG. 6C

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1 GAATTCAACT TCTCCATPACT TTGGATAGG AATACAGAC ATGAARAATC TCATTGCTGA GTTGTATTTT AAGTTGCCC AAAAGAAGA AGACTCGAAT
CTTAAGTTGA AGAGGTATGA AACCTATTCC TTTATGTCGT TACTTTTAG AGTAACGACT CACAAATAA TTCGAACGGG TTTTCTTCT TCTCAGCTTA

101 GAACGTGTG CACAGGTAGA AGCTTTGGAG ATTATGCTCA CTGCAATGCT TCGCAATATG GGCACAAATG ACCAACAGCG GTTGATTGAT CAGGTAGAGG
CTTGACACAC GCGTCCATCT TCGAAACCTC TAATAGCAGT GAGTTACGA AGCGTTATAC CGCGTTTAC TGGTTGTGCG CAACTAACTA GTCCATCTCC

201 GGGCGCTGA CAGGTAAAG CCGATGCCA GCATTCTCTGA CGAGTATCG GAGCTGCTGC GCGATTACGT AAAGAAGTTA TTGAAGCATC CTGCTCAGTA
CCCGGACAT GCTCCATTTT GGGCTACGGT CGTAAGGACT GCTGCTATGC CTCGACGAGC CGCTAATGCA TTTCTTCAAT AACTTCGTAG GAGCAGTCAT

301 AAAAGTTAAT CTTTCAACA GCTGTCTATA AGTTGTACG GCGGAGACTT ATAGTCGCTT TGTTTTATT TTTTAATGTA TTGTAACTA GTACGCAAGT
TTTTCAATTA GAAAGTTGT CGACAGTATT TCAACAGTGC CGGCTCTGAA TATCAGCGAA ACAAAATAA AAAATTACAT AAACATTGAT CATGCGTTCA

401 TCACGTAAAA AGGTATCTA GAATTATGAA AAAGAATATC GCATTTCTTC TTGCATCTAT GTTCGTTTTT TCTATTGCTA CAAACGCGTA CGCTGATATC
AGTGCATTTT TCCCATAGAT CTTAATACTT TTCTTATAG CGTAAAGAG AACGTAGATA CAAGCAAAA AGATAACGAT GTTTGCGCAT GCGACTATAG

1 M K K N I A F L L A S M F V F S I A T N A Y A D I
^Start STII signal TIR 7 anti-tissue factor light chain^

501 CAGATGACCC AGTCCCGAG CTCCTGTGTC GCTCTGTGG GGGATAGGT CACCATCACC TGCAGAGCCA GTCCGACAT CAAGAGCTAT CTGAACGTGGT
GTCTACTGG TCAGGGGCTC GAGGGACAGG CCGGACACCC CGCTATCCCA GTGCTAGTGG AGTCTCGGT CAGCGCTGTA GTTCTCGATA GACTTGACCA

26 Q M T Q S P S L S A S V G D R V T I T C R A S R D I K S Y L N W Y

601 ATCAACAGAA ACCAGGAAA GCTCCGAAAG TACTGATTTA CTATGTACT AGTCTGCTG AAGGAGTCCC TTCTCGCTTC TCTGATCCG GTTCTGGGAC
TAGTTGTCTT TGGTCCCTTT CGAGGCTTTC ATGACTAAT GATACATGA TCAGAGCAC TTCTCAGGG AAGAGCGAAG AGACCTAGGC CAAGACCGTG

60 Q Q K P G K A P K V L I Y Y A T S L A E G V P S R F S G S G T

701 GGATTACACT CTGACCATCA GCAGTCTGCA GCCAGAAGAC TTCGCAACTT ATTACTGTCT TCAGCACGGA GAGTCTCCAT GGACATTTGG ACAGGGTACC
CCTAATGTGA GACTGGTAGT CGTCAGACGT CGGTCTTCTG AAGCGTTGAA TAATGACAGA AGTCTGCTC CTCAGAGGTA CCTGTAAACC TGTCCCATGG

93 D Y T L T I S S L Q P E D F A T Y Y C L Q H G E S P W T F G Q G T

801 AAGTGGAGA TCAACGAACT TGTGGCTGCA CCATCTGTCT TCATCTTCCC GCCATCTGAT GAGCAGTTGA AATCTGGAAC TGTCTCTGTT GTGTGCTGTC
TTCCACCTCT AGTTTGCTTG ACACCGACGT GGTAGACAGA AGTAGAAGG CGGTAGACTA CTCGTCAACT TTAGACCTTG ACGAAGACAA CACACGAGC

126 K V E I K R T V A A P S V F I F P P S D E Q L K S G T A S V V C L L

901 TGAATTAATT CTATCCAGA GAGGCCAAG TACAGTGAA GGTGATAAC GGCCTCCAAT CCGGTAACTC CCAGGAGAGT GTACAGAGC AGGACAGCAA
ACTTATTGAA GATAGGGTCT CTCGGTTTC ATGTCACCTT CCACCTATTG CCGGAGGTTA GCCCATTTAG GTCCTCTCA CAGTGTCTCG TCCGTGCTT

160 N N F Y P R E A K V Q W K V D N A L Q S G N S Q E S V T E Q D S K

1001 GGACAGCACC TACAGCCTCA GCAGCACCT GAGCTGAGC AAAGCAGACT ACGAAGACA CAAAGTCTAC GCCTGGAAG TCACCCATCA GGGCCTGAGC
CCTGCTGG AGTCGGAGT CGTCGGTGGG CTGCGACTCG TTTGCTCTCA TGCTCTTGT GTTTCAGATG CGGACGCTTC AGTGGGTAGT CCGGACTCG

193 D S T Y S L S S T L T L S K A D Y E K H K V Y A C E V T H Q G L S

FIG. 7A

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1101 TCGCCCGTCA CAAAGAGCTT CAACAGGGGA GAGTGTAAAT TAAATCTCT AGCCGGAGC CATCTGGTAC CCGGGGATCT AGGCTAAAG
AGCGGGCAGT GTTCTCGAA GTTGTCCCT CTCACATTA ATTAGGAGA TCGGGCTGC GTAGCACGC TCGAGCCATG GCGCCCTAGA TCCGATTGC
226 S P V T K S F N R G E C O
lambda t0 terminator
1201 CTCGGTTGCC GCGGGGGTT TTTTATTGT GCGAGCGC ATCTCGACTG CACGTCAC CAATGCTTCT GGCGTCAGC AGCATCGGA AGCTGTGTA
GAGCAACCG CGGCCCGCAA AAAATAACAA CGGCTGCGG TAGAGCTGAC GTGCCAGTG GTTACGAAGA CCGAGTCCG TCGTAGCCT TCGACACCAT
1301 TGGCTGTGCA GGTGCTAAAT CACTGCATTA TTGCTGTGC TCAAGGCGA CTCCGCTTCT GGATAATGTT TTTTGGCGG ACATCATAAC GGTCTGGCA
ACCGACACGT CCAGCATTTA GTGAGTAIT AAGCACAGCG AGTTCCGGT GAGGCAAGA CCTATTCAA AAAACGCGG TGTAGTATTG CCAAGACCGT
1401 AATATTCTGA AATGAGCTGT TGACATTA TCAATGAAT AGTTTAACT GTGGAATGT GAGCGGATA CAATTAAGCT TAGGATCTAG AATTATGAAG
TTATAAGACT TTAATCGACA ACTGTAAIT AGTAGCTTGA TCAATTAACA CACCTTAACA CTGCTTATT GTTAATCGA ATCTAGATC TTAATACATTC
1 Start M K
anti-tissue factor heavy chain with cys to ser in hinge
Start STII signal TIR 3
1501 AAGAAATATTG CGTTCCTACT TGCCTCTATG TTTGTCTTTT CTATAGCTAC AAACGGCTAC GCTGAGTTT AGCTGGTGA GTCTGGCGT GGCCTGGTGC
TTCTTATAAC GCAAGGATGA ACGGAGATAC AAACAGAAA GATATCGATG TTTGCGCATG CGACTCCAAG TCGACACCAT CAGACCCCA CCGGACCAG
3 K N I A F L L A S M F V F S I A T N A Y A E V Q L V E S G G L V Q
anti-tissue factor heavy chain with cys to ser in hinge
1601 AGCCAGGGG CTCACCTCGT TTGCTCTGT CAGCTTCTG CTTCATATT AAGAGTACT ACATGCACTG GGTCCGTGAG GCGCCGGGA AGGCTCTGA
TCGTCCCGG GAGTGAGCA AACAGGACAC GTCGAAGACC GAAGTTATAA TTCTCATGA TGTACGTGAC CCAGGACATC CCGGGCCCAT TCCCGGACCT
37 P G G S L R L S C A A S G F N I K E Y Y M H W V R Q A P G K G L E
1701 ATGGTTTGA TTGATTGATC CAGAGCAAGG CAAACAGATC TATGACCGA AGTTCCAGGA CCGTSCCAT ATAAAGCTG ACAATTCOA AAACACAGA
TACCAACCT AACTAACTAG GTCTCGTTCC GTTGTGCTAG ATACTGGCT TCAAGTCTT GGCACGTGA TATTGCGAC TGTAAAGTT TTTGTGCTG
70 W V G L I D P E Q G N T I Y D P K F Q D R A T I S A D N S K N T A
1801 TACCTGCAGA TGAACAGCT CCGTCTGAG GACACTCCG TCTATTATTG TCTCGAGAC ACGCCGCTT ACTTCGACTA CTGGGGTCAA GGAACCTGG
ATGAGCTCT ACTTGTGGA CGCAGACTC CTGTGACGC AGATAATAC AGAGTCTG TCGCGGCGAA TGAAGTGTG TGAAGTGTG TGAAGTGTG TGAAGTGTG
103 Y L Q M N S L R A E D T A V Y Y C A R D T A A Y F D Y W G Q G T L V
1901 TCACCGTCT CTCGGCTCC ACCAAGGCC CATCGTCTT CCGCTGGA CCGCTCTCCA AGAGCACCTC TGGGGGACA GCGGCCCTGG GCTGCTGCT
AGTGCAGAG GAGCGGAGG TGGTTCCCG GTAGCCAGAA GGGGACCGT GGGAGAGGT TCTGTTGAG ACCCGCTGT CCGCGGACC CGACGAGCA
137 T V S S A S T K G P S V F P L A P S S K S T S G G T A A L G C L V
2001 CAAGGACTAC TTCCCGAAC CGGTGACGCT GTCGTGAAC TCAGCGGCC TGACACAGCG CGTCCACACC TTCCCGGCTG TCCTACAGTC CTCAGGACTC
GTTCTGATG AAGGGGCTG GCCACTGCC CAGCACCTTG AGTCGCGGG ACTGTGCGC GCAGTGTGG AAGGCGGAC AGGATGTGAG GAGTCTGAG
170 K D Y F P E P V T V S W N S G A L T S G V H T F P A V L Q S S G L
2101 TACTCCCTCA GCAGCTGCT GACTGTGCC GACTGTGCC TCTAGAGCT TGGGACCCA GACCTACATC TGCAACGTGA ATCAAGCC CAGCAACACC AAGTGGACA
ATGAGGAGT CGTGCACCA CTGACACGG AGATCTGGA ACCGTGGT CTGATGTAG ACGTTGACT TAGTGTGCTG GTGTTGCTG TCCACCTGT
203 Y S L S S V V T V P S S S L G T Q T Y I C N V N H K P S N T K V D K

FIG. 7B

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2201 AGAAGATTGA GCCAATATCT TGTGACAAA CTCACACTAG TCCACCGTCT CCAGCACCTG AACTCCTGGG GGGACCGTCA GTCTTCTCTT TCCCCCAAA
TCITTCACT CGGGTTTGA ACACGTGTTT GAGTGTGATC AGGTGGCAGA GGTCTGGAC TTGAGGACCC CCCTGGCAGT CAGAAGAGA AGGGGGTTT
237 K V E P K S C D K T H T S P P S P A P E L L G G P S V F L F P P K
^Hinge cys to ser ^Hinge cys to ser
2301 ACCCAAGGAC ACCCTCATGA TCTCCCGGAC CCTGAGTGC ACATGCGTGG TGGTGGACGT GAGCCACGAA GACCTGAGG TCAAGTTCAA CTGTTACGTG
TGGGTCTCTG TGGGAGTACT AGAGGCCCTG GGGACTCCAG TGATACGACCC ACCACTGCA CTCGGTCTCT CTGGACTCC AGTTCAAGTT GACCATGCAC
270 P K D T L M I S R T P E V T C V V V D V S H E D P E V K F N W Y V
2401 GACGCGTGG AGGTGCATAA TGCCAAGACA AAGCCGCGG AGGACGACTA CAACAGCAG TACCGTGGG TCAGGCTCTT CACCGTCTG CACGAGACT
CTGCGGCACC TCACAGTATT ACGTTCTGT TTCGGGCCCC TCCTGCTCAT GTTGTGTCG ATGGCACCC AGTCCAGGA GTGGCAGGAC GTGGTCTCTGA
303 D G V E V H N A K T K P R E E Q Y N S T Y R V V S V L T V L H Q D W
2501 GGCTGAATGG CAAGGAGTAC AAGTCAAGG TCTCCAACA AGCCCTCCCA GCGCCCATCG AGAAACCAT CTCNAAGCC AAAGGGCAGC CCCGAGAACC
CCGACTTACC GTTCTCTCATG TTCAGTTTCC AGAGGTTGTT TCGGGAGGCT CGGGGTAGC TCCTTTGGTA GAGGTTTCGG TTTCCTCGTC GGGCTCTTGG
337 L N G K E Y K C K V S N K A L P A P I E K T I S K A K G Q P R E P
2601 ACAGGTGTAC ACCCTGCCCC CATCCCGGA AGAGATGACC AAGRACCAGG TCAGCTGAC CTGCTGCTC AAAGCTTCT ATCCCAGCA CATCGCCGTG
TGTCCACATG TGGGACGGG GTAGGCCCT TCTCTACTGG TTCTGTGTC AGTCCGACTG GACGGACAG TTTCGAAGA TAGGTCGCT GTAGCGGAC
370 Q V Y T L P P S R E E M T K N Q V S L T C L V K G F Y P S D I A V
2701 GAGTGGGAGA GCAATGGCA GCGGAGAAC AACTACAAGA CCAGCCCTCC CGTGTGGAC TCCGACGGCT CCTTCTTCT CTACAGCAAG CTCACCGTGG
*CTCACCTCT CGTTACCCGT CGGCTCTTGG TTGATGTTCT GGTGCGGAGG GCACGACCTG AGGCTGCCGA GGAAGAAGA GATGCTGTTT GAGTGGCACC
403 E W E S N G Q P E N N Y K T T P P V L D S D G S F L Y S K L T V D
2801 ACAAGAGCAG GTGGCAGCAG GGGAACGTCT TCTCATGCTC CGTGATGCAT GAGGTCTGC ACAACCACTA CACGACAGA AGCTCTCTCC TGCTCCGGG
TGTTCTGTC CACCGTCGTC CCTTGCAGA AGAGTAGGAG GACTACGTA CTCGAGACG TGTGTGATG GTGCTCTTTC TCGGAGAGG ACAGAGGCC
437 K S R W Q Q G N V F S C S V M H E A L H N H Y T Q K S L S L S P G
2901 TAAATAAGCA TGGGACGGCC CTAGAGTCCC TAAAGTCCG TTGCGCGCGG CGGTTTTTTA TTGTTAACTC ATGTTTGACA GCTTATCATC GATAAGCTTT
ATTATTCTGT ACGCTGCCGG GATCTCAGG ATTGCGAGCC AACGGCGGCC CGCAAAAAT AACAAATTAG TACAACTGT CGAATAGTAG CTATTGAAA
470 K O
3001

FIG. 7C

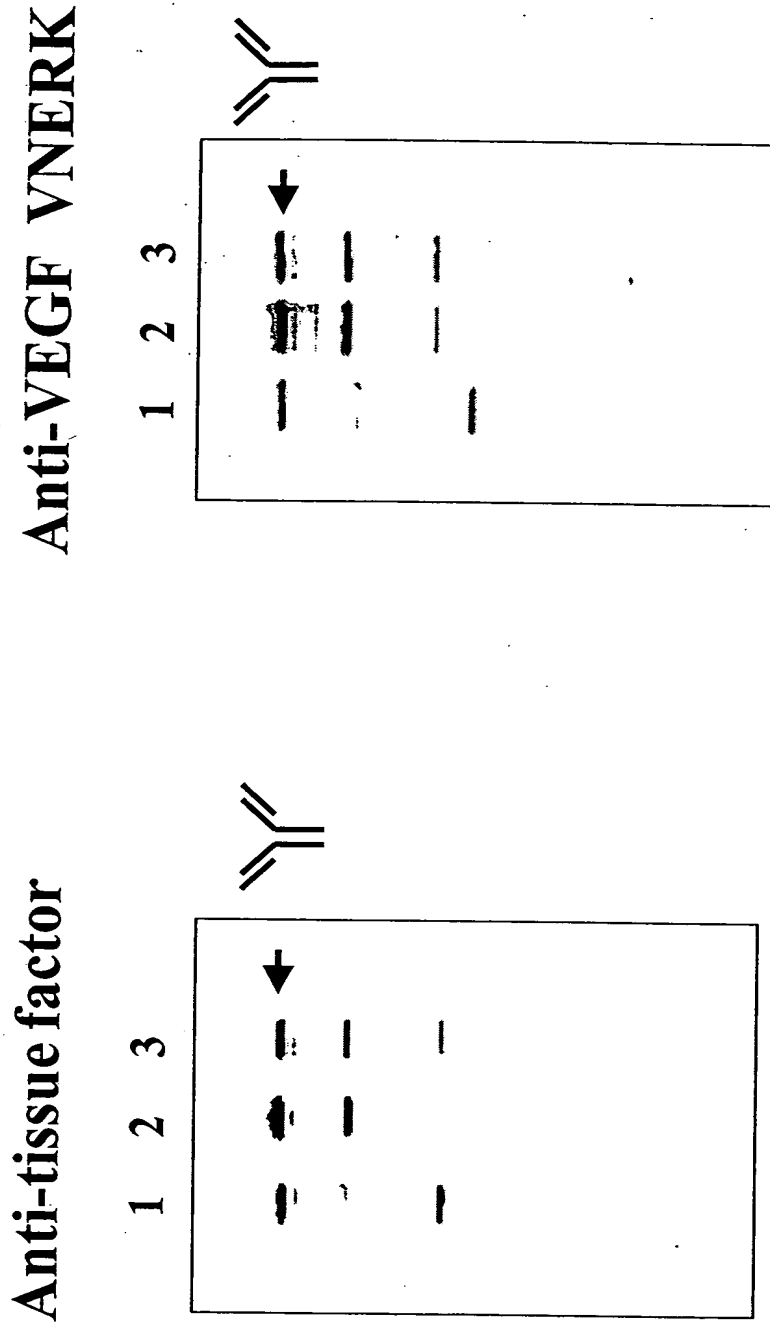


FIG. 8

Anti-tissue factor Anti-VEGF-VNERK

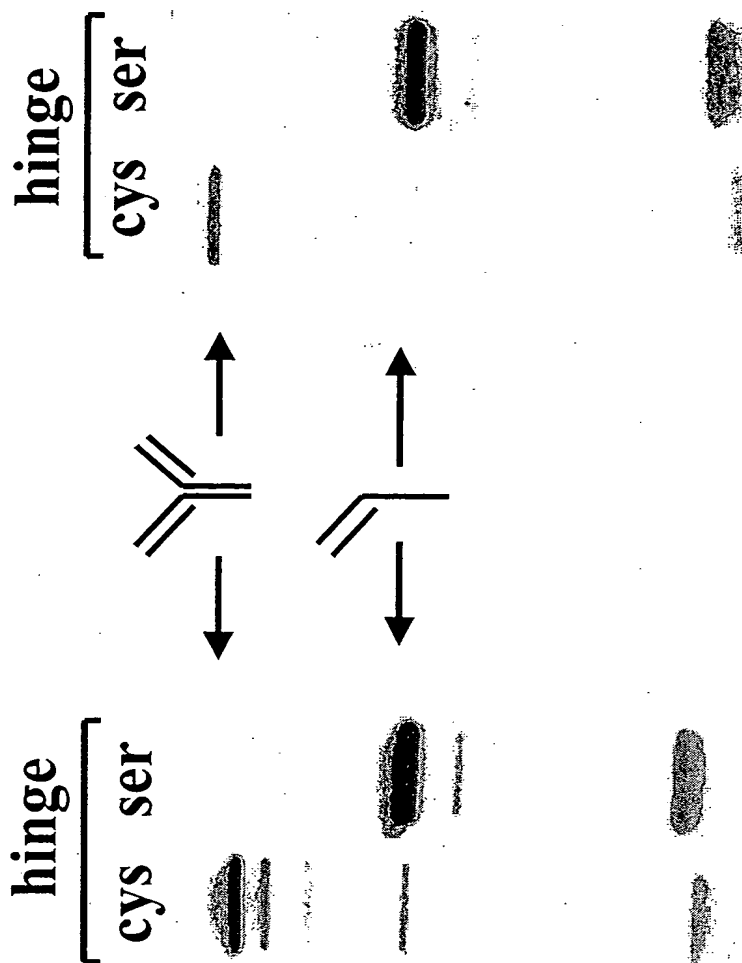


FIG. 9

Anti-VEGF-Y0317

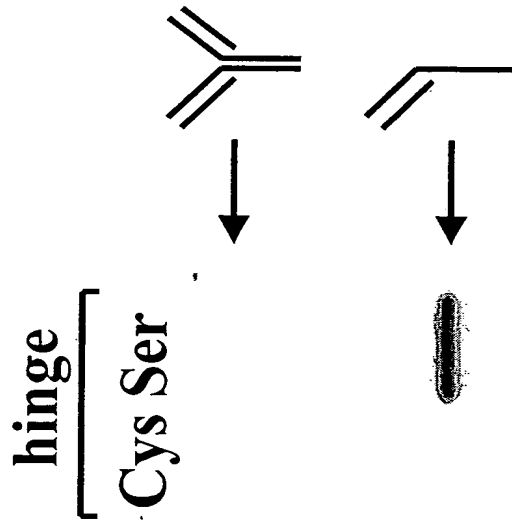


FIG. 10

murine Flt-IgG2b

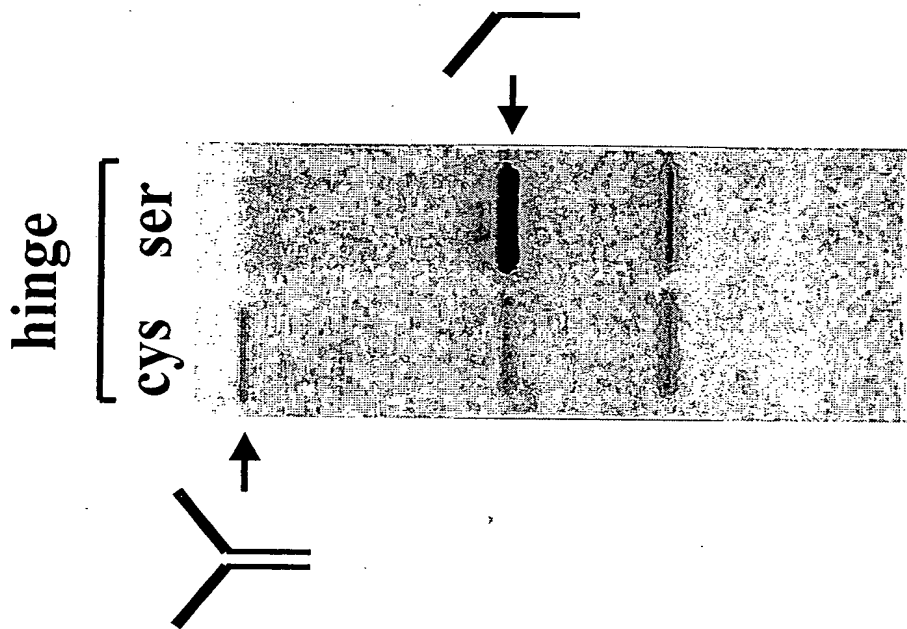


FIG. 11

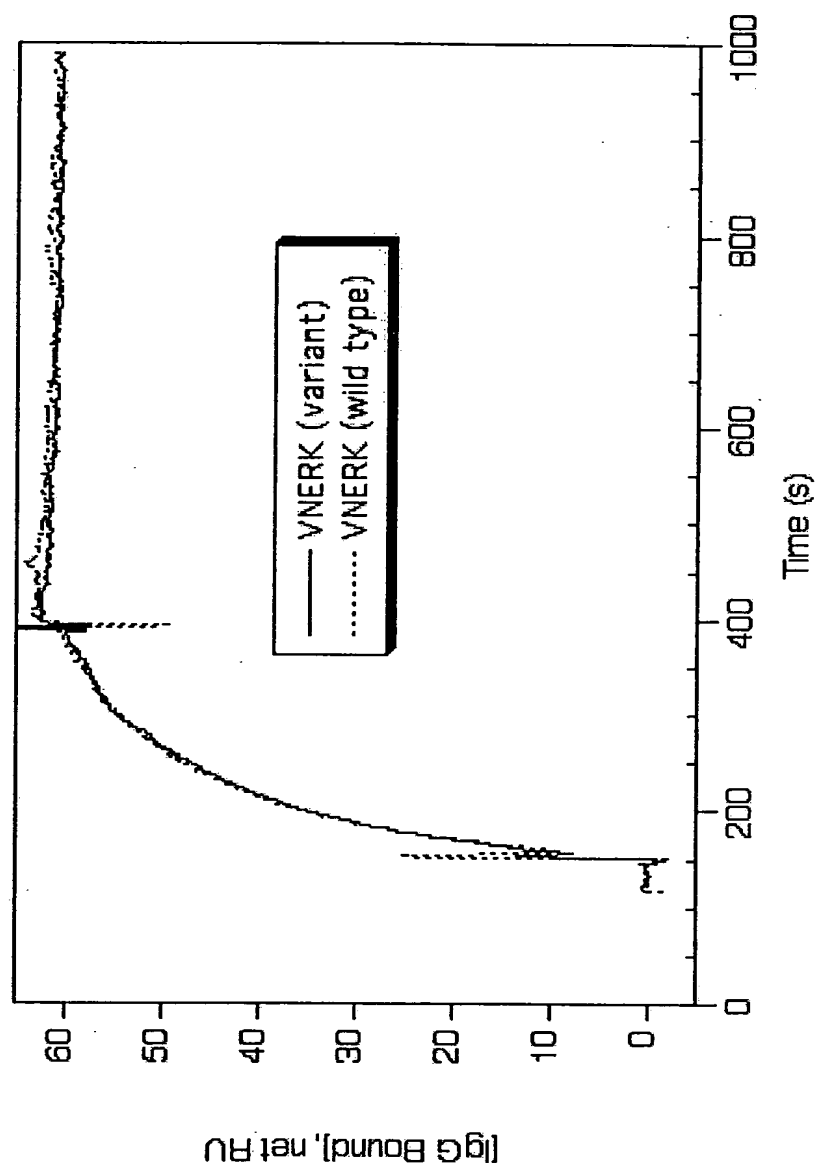


FIG. 12

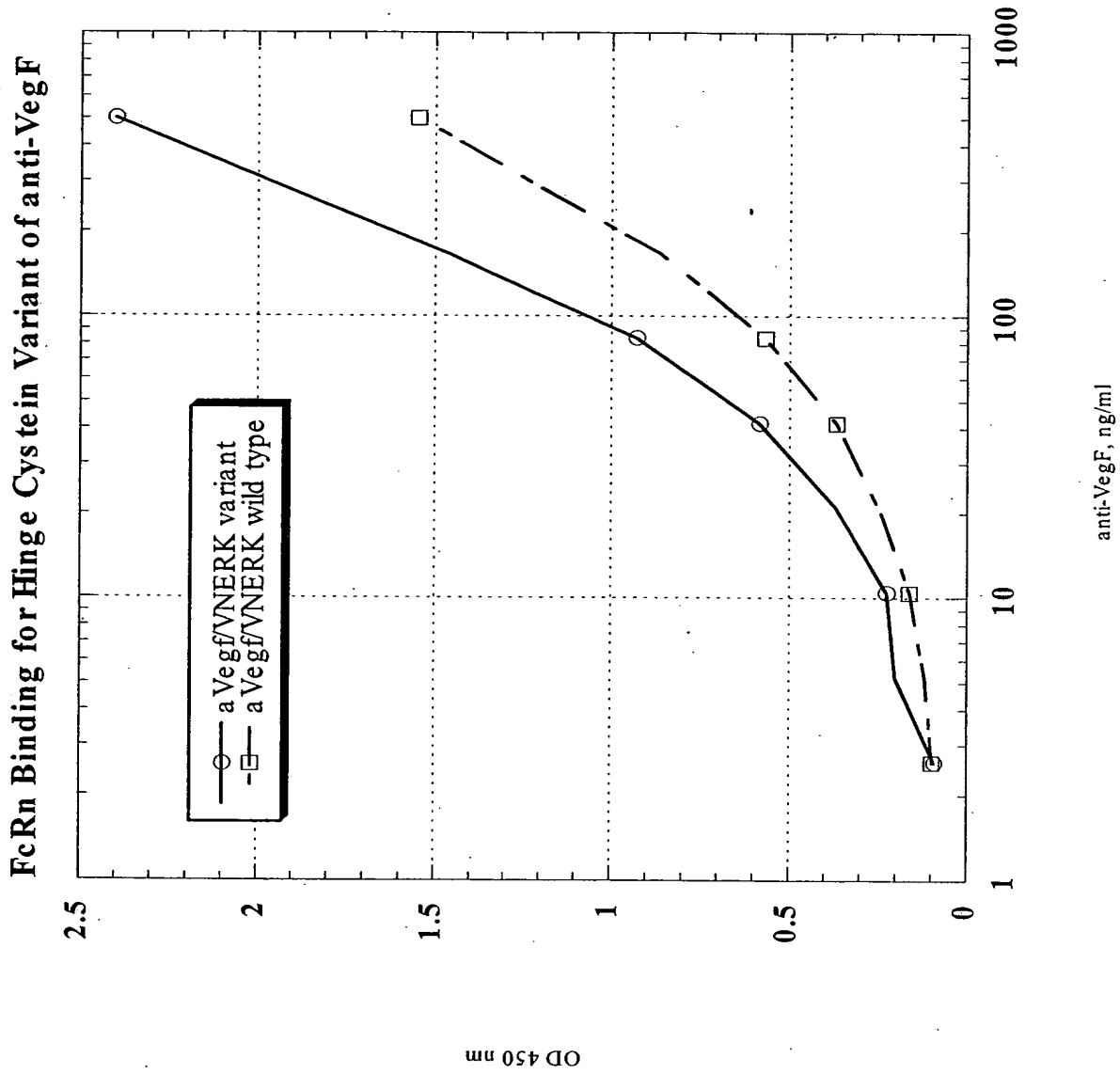


FIG. 13

FcRn Binding of Hinge Cysteine Mutants of anti-Tissue Factor

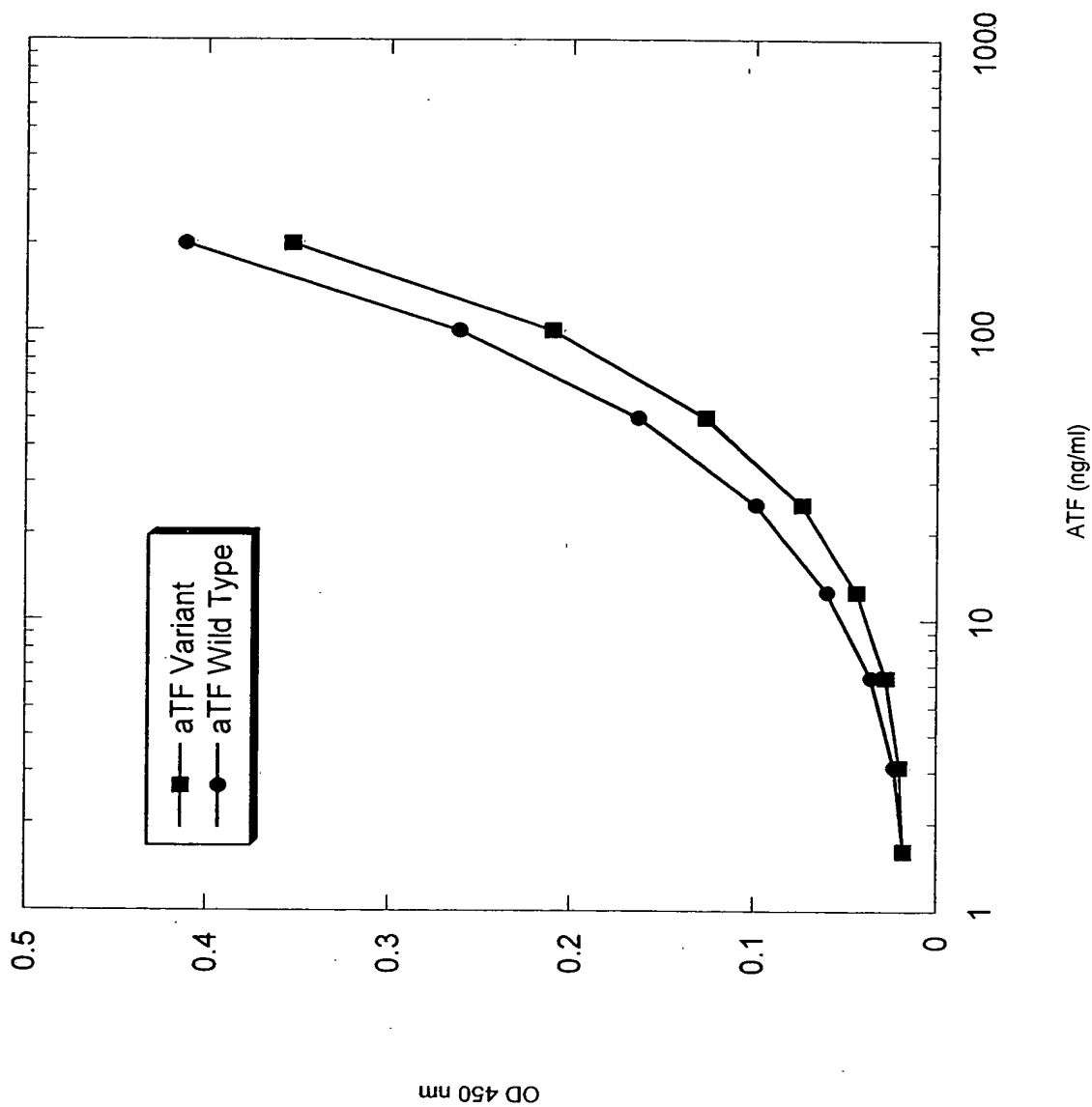


FIG. 14

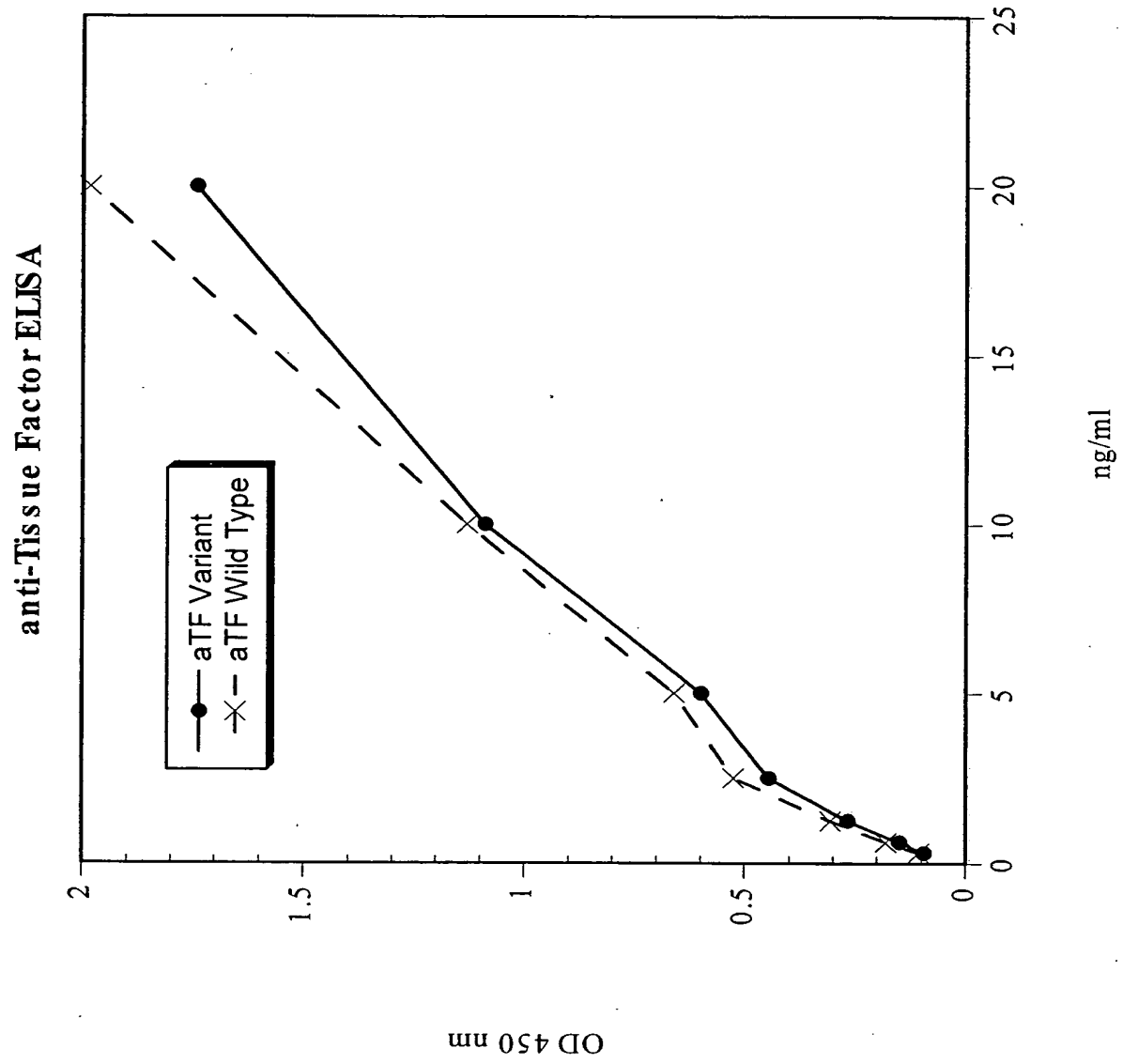


FIG. 15

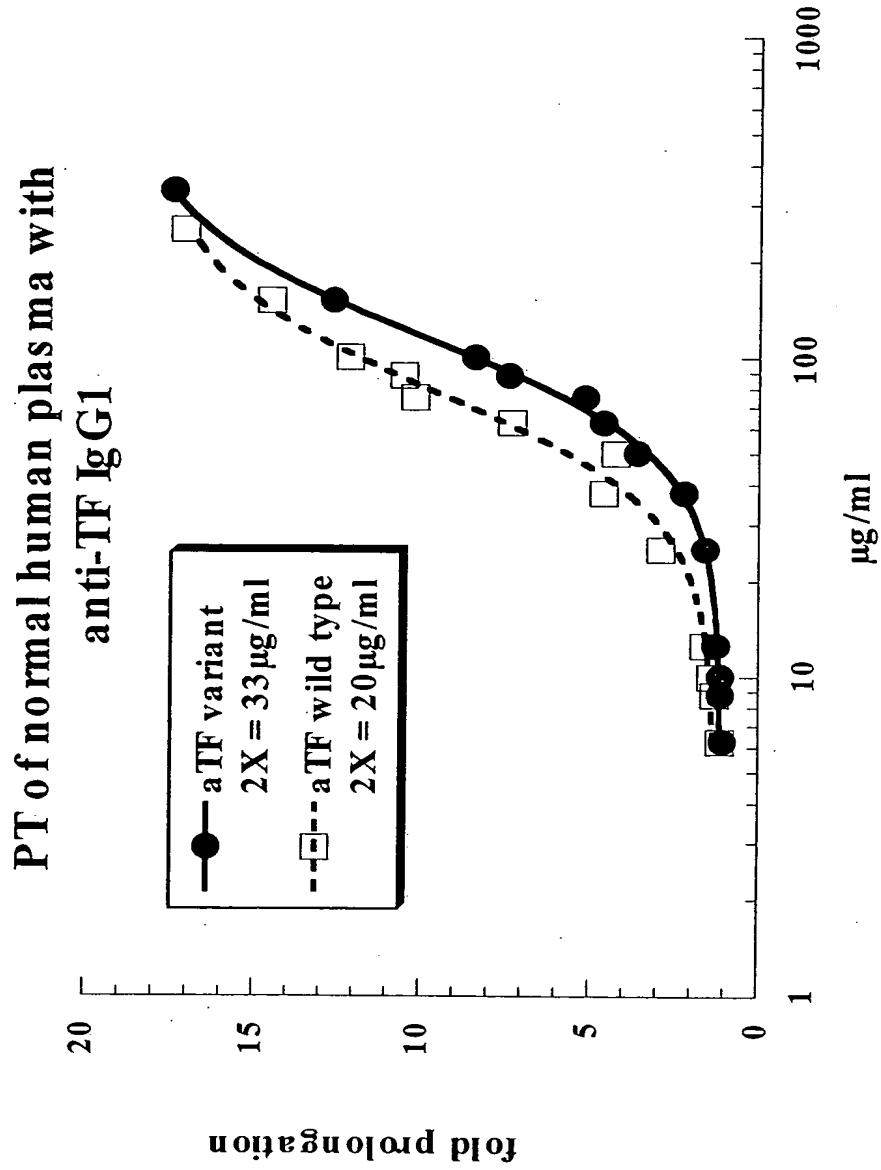


FIG. 16

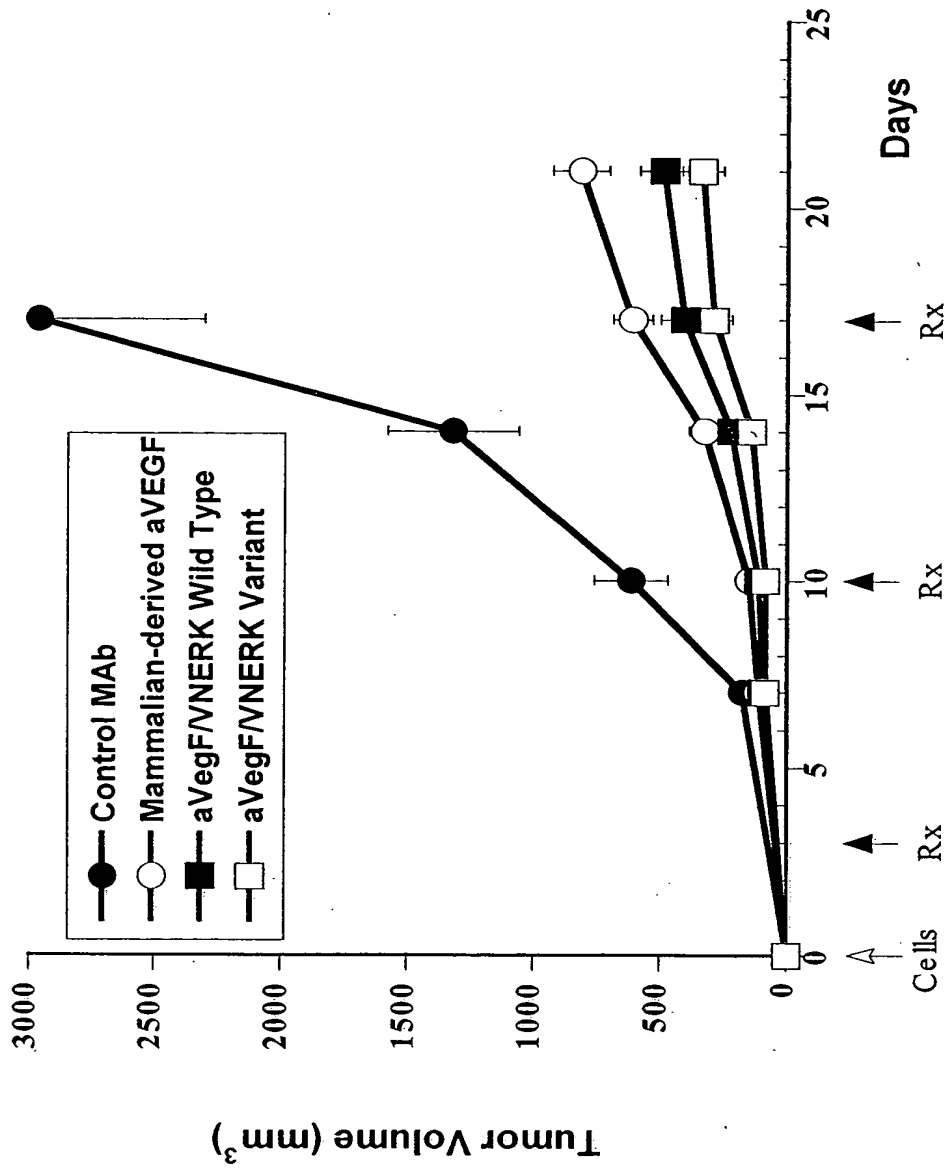


FIG. 17

Inhibition of Growth of A673 Tumors

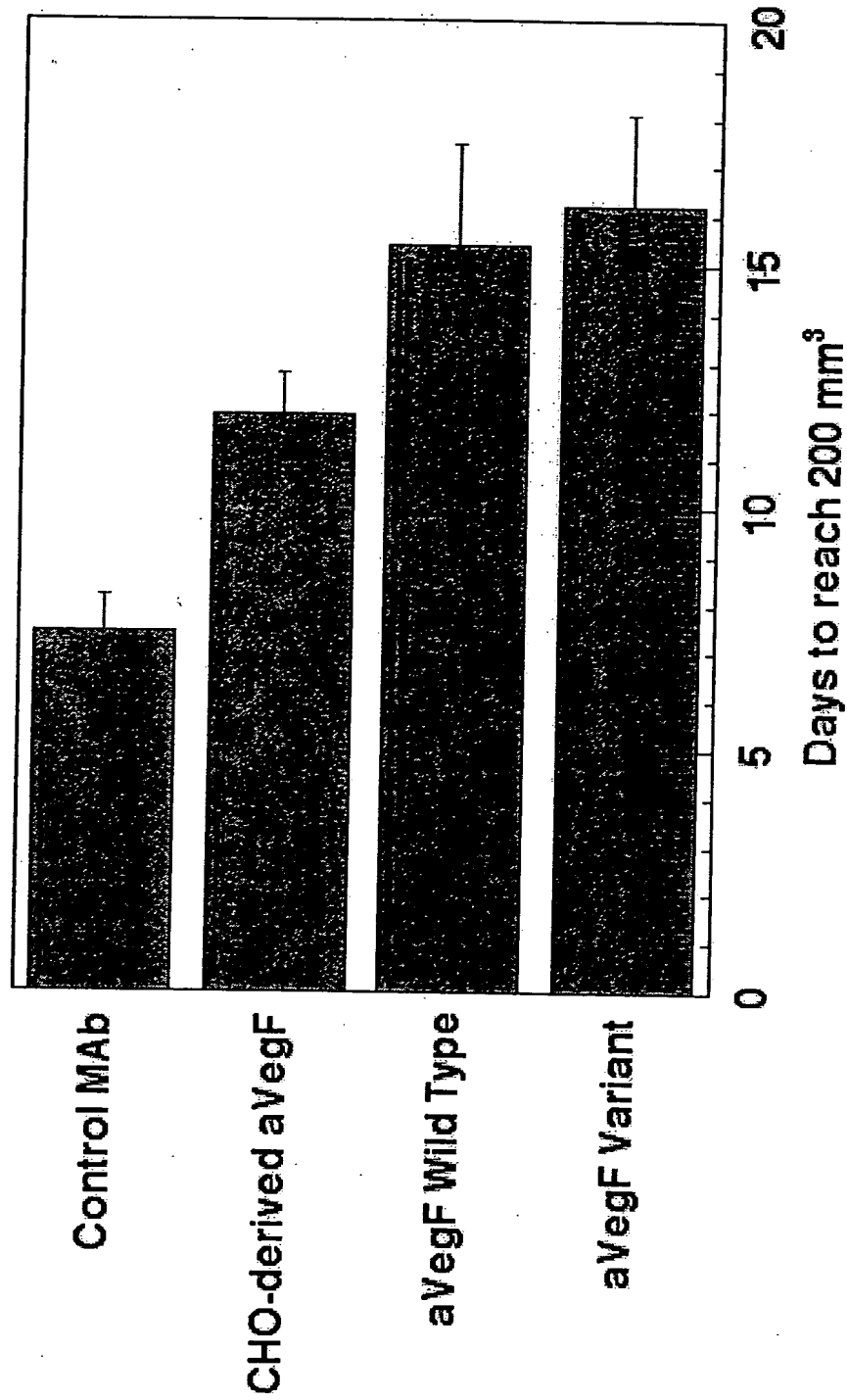


FIG. 18

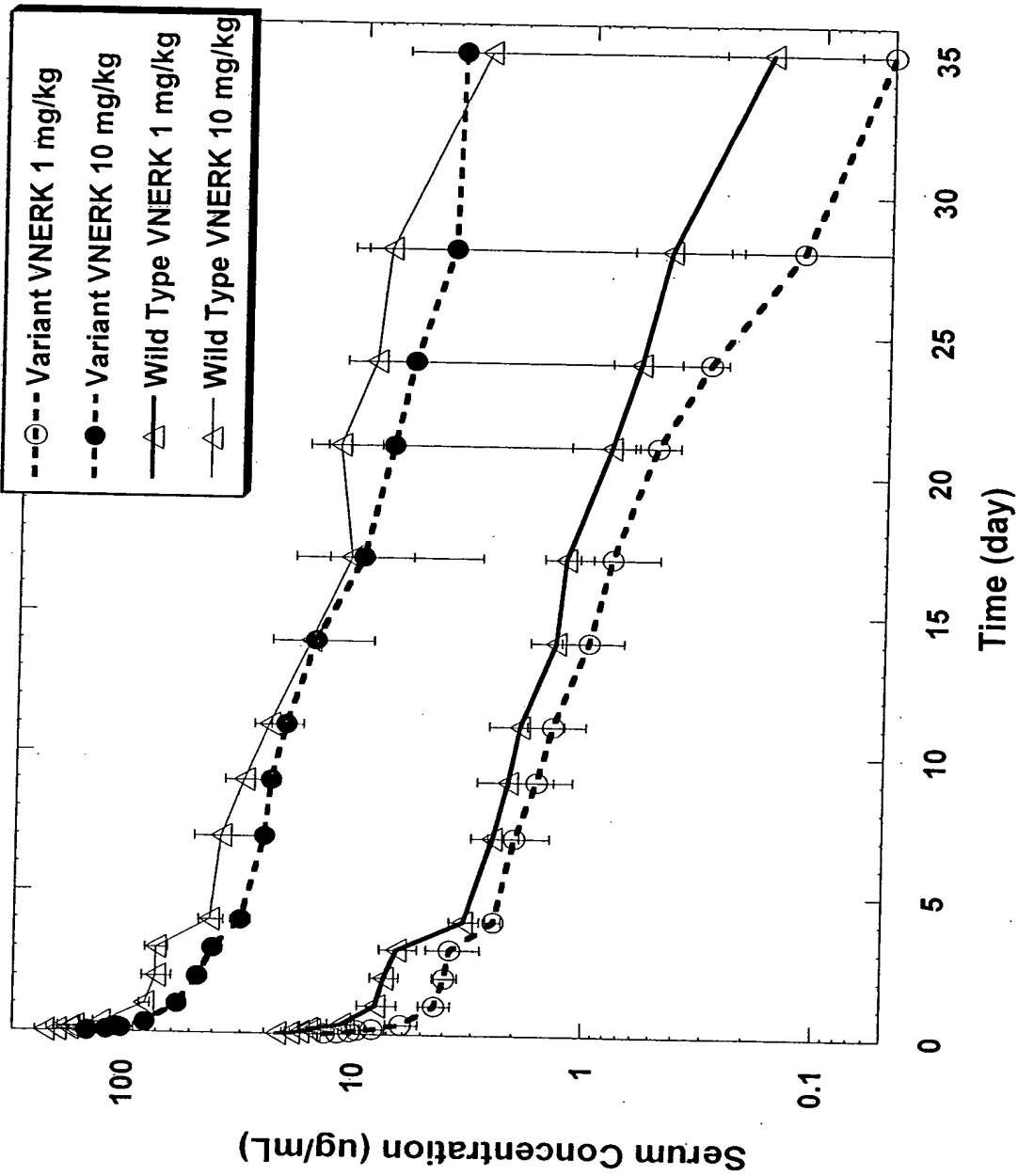


FIG. 19